```
=> d his

     (FILE 'HCAPLUS' ENTERED AT 12:17:46 ON 04 JAN 2001)
                DEL  HIS
                E WO9830902/PN
L1            1 S E3
L2         2019 S DNA LIGASE
L3           53 S DNA LIGASE IV

     FILE 'REGISTRY' ENTERED AT 12:19:22 ON 04 JAN 2001
L4            1 S 9015-85-4
                SEL CHEM

     FILE 'HCAPLUS' ENTERED AT 12:19:52 ON 04 JAN 2001
L5         1225 S L4
L6         3171 S E1-E24
L7           22 S POLYDEOXYRIBONUCLEOTIDE()(SYNTHETASE OR SYNTHASE)
L8            0 S POLYNUCLEOTIDE SYNTHASE
L9         3173 S L2,L3,L5-L8
                E L1 AU
                E JACKSON S/AU
L10          90 S E3,E19
L11         111 S E99,E109,E110
L12           1 S E123
                E CRITCHLOW S/AU
L13           8 S E5,E9,E10
L14           6 S L9 AND L10-L13

     FILE 'REGISTRY' ENTERED AT 12:27:03 ON 04 JAN 2001
L15          85 S DNA LIGASE
L16          84 S L15 NOT L4

     FILE 'HCAPLUS' ENTERED AT 12:27:27 ON 04 JAN 2001
L17       10753 S L16
L18           2 S L17 AND L10-L13
L19           6 S L14,L18
L20          60 S XRCC4
L21           6 S L10-L13 AND L20
L22           5 S L19 AND L21
L23           2 S L19,L21 NOT L22
L24           7 S L22,L23
L25        3017 S DNA (L) LIGASE
L26         106 S DNA (L) LIGASE (L) IV
L27           1 S DNA (L) LIGASEIV
L28           6 S L10-L13 AND L25-L27
L29           7 S L24,L28
L30           9 S PKCS KU
L31           1 S L10-L13 AND L30
L32           7 S L29,L31
L33       14116 S L9,L17,L25-L27
L34           2 S L33 AND L30
L35          58 S L33 AND PK##
L36          28 S L33 AND KU
L37          36 S L30,L35-L36,L33 AND L20
L38           8 S L32,L34
L39          31 S L37 NOT L38
L40          39 S L38,L39
L41          39 S L40 AND DNA
L42           3 S L40 AND CDNA
L43           1 S L40 AND MRNA
L44           1 S L40 AND (DEOXYRIBONUCLE? OR RIBONUCLE?)
L45          39 S L40-L44
L46          23 S L20 NOT L45
L47          62 S L45,L46,L32,L38
L48          17 S L47 AND (PD<=19970113 OR PRD<=19970113 OR PRD.B<=19970113 OR
```

Point of Contact:
Jan D...
Librari...
C...

```
L49           4 S L29 NOT L48
L50          21 S L48,L49
L51          21 S L50 AND L9,L17,L20,L25-L27,L30
L52          11 S L50 AND (KU## OR PK##)
L53          21 S L51,L52
L54       14116 S L9,L17,L25-L27
L55       11791 S L54 AND (PD<=19970113 OR PRD<=19970113 OR PRD.B<=19970113 OR
L56          28 S L55 AND DRUG(S)SCREEN?
L57           4 S L56 AND L5
L58           3 S L56 AND L2
L59           1 S L56 AND L3
L60           4 S L56 AND L6
L61           0 S L56 AND L7
L62           7 S L56 AND L25-L27
L63           8 S L57-L62
L64           5 S L63 AND (ASSAYS OR KU(2W)REPAIR OR SCREENING)/TI
L65           3 S L64 NOT (RACEMASE OR AVIUM)/TI
L66          23 S L53,L65
L67          20 S L56 NOT L63,L66
L68          22 S L55 AND DRUG(S)DESIGN?
L69          46 S L68,L56
L70          38 S L69 NOT L63,L66
L71           2 S L70 AND LIGASE
L72          25 S L66,L71
                SEL RN L32

     FILE 'REGISTRY' ENTERED AT 12:58:09 ON 04 JAN 2001
L73           8 S E1-E8
L74           1 S 56-65-5
L75           6 S L73 NOT L74,L4
L76           3 S XRCC4
L77         125 S POLYDEOXYRIBONUCLEOTIDE (S) SYNTHETASE
L78           6 S L77 (S) IV
L79           9 S L76,L78
L80           2 S L75 NOT L79

     FILE 'HCAPLUS' ENTERED AT 13:01:51 ON 04 JAN 2001
L81           6 S L79
L82          28 S L72,L81
L83           3 S L82 NOT L72
L84          28 S L82,L83

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:03:20 ON 04 JAN 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1967 - 4 Jan 2001  VOL 134 ISS 2
FILE LAST UPDATED: 3 Jan 2001  (20010103/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

 This file supports REGlstRY for direct browsing and searching of
 all substance data from the REGISTRY file.  Enter HELP FIRST for
 more information.

Now you can extend your author, patent assignee, patent information,
```

and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.

=> d l84 bib abs hitrn tot

L84 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:203210 HCAPLUS
DN 133:101453
TI Comparison of DNA repair protein expression and activities between human fibroblast cell lines with different radiosensitivities
AU Carlomagno, Francesca; Burnet, Neil G.; Turesson, Ingela; Nyman, Jan; Peacock, John H.; Dunning, Alison M.; Ponder, Bruce A. J.; **Jackson, Stephen P.**
CS CRC Human Cancer Genetics Group, University of Cambridge, Cambridge, CB1 8RN, UK
SO Int. J. Cancer (2000), 85(6), 845-849
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB In order to investigate the mol. basis of variation in response to ionizing radiation (IR) in radiotherapy patients, we have studied the expression of several genes involved in **DNA** double-strand break repair pathways in fibroblast cell lines. Ten lines were established from skin biopsies of cancer patients with different normal-tissue reactions to IR, and 3 from a control individual. For all 10 test cell lines, the cellular radiosensitivity was also known. Using Western blots we measured, in non-irradiated cells, the basal expression levels of ATM, Rad1 and Hus1, involved in the control of cellular **DNA** damage checkpoints, together with **DNA-PKcs**, **Ku70**, **Ku80**; **XRCC4**, **ligaseIV** and Rad51, involved in radiation-induced DSB repair. We also analyzed the in vitro enzymic activities, under non-irradiated conditions, of the **DNA-PK** and **XRCC4/ligaseIV** complexes. The levels of expression of the different proteins were similar in all the cell lines, but the activities of the **DNA-PK** and **XRCC4/ligaseIV** complexes showed some differences. These differences did not correlate with either the normal tissue response of the patient in vivo or with cellular radiation sensitivity in vitro. The activity differences of these enzyme complexes, therefore, do not account for the variation of responses seen between patients.
IT **9015-85-4, Dna Ligase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**XRCC4** complex; comparison of **DNA** repair protein expression and activities between human fibroblast cell lines with different radiosensitivities)
RE.CNT 19
RE
(2) Baumann, P; Cell 1996, V87, P757 HCAPLUS
(6) Critchlow, S; Curr Biol 1997, V7, P588 HCAPLUS
(7) Critchlow, S; Trends Biochem Sci 1998, V23, P394 HCAPLUS
(8) Freire, R; Genes Develop 1998, V12, P2560 HCAPLUS
(10) Hartley, K; Cell 1995, V82, P849 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:129227 HCAPLUS
DN 132:247685
TI Lif1p targets the **DNA ligase** Lig4p to sites of **DNA** double-strand breaks
AU Teo, Soo-Hwang; **Jackson, Stephen P.**
CS The Wellcome Trust and Cancer Research Campaign, Institute of Cancer and Developmental Biology, University of Cambridge, Cambridge, CB2 1QR, UK

SO Curr. Biol. (2000), 10(3), 165-168
CODEN: CUBLE2; ISSN: 0960-9822
PB Elsevier Science Ltd.
DT Journal
LA English
AB **DNA ligases** catalyze the joining of **DNA** single- and double-strand breaks. Saccharomyces cerevisiae Cdc9p is a homolog of mammalian **DNA ligase** I and is required for **DNA** replication, recombination and single-strand break repair. The other yeast **ligase**, Lig4p/Dnl4p, is a homolog of mammalian **DNA ligase IV**, and functions in the non-homologous end-joining (NHEJ) pathway of **DNA** double-strand break repair [1-4]. Lig4p interacts with Lif1p, the yeast homolog of the human **ligase IV**-assocd. protein, **XRCC4** [5]. This interaction takes place through the carboxy-terminal domain of Lig4p and is required for Lig4p stability. We show that the carboxy-terminal interaction region of Lig4p is necessary for NHEJ but, when fused to Cdc9p, is insufficient to confer NHEJ function to Cdc9p. Also, Lif1p stimulates the in vitro catalytic activity of Lig4p in adenylation and **DNA** ligation. Nevertheless, Lig4p is inactive in NHEJ in the absence of Lif1p in vivo, even when Lig4p is stably expressed. We show that Lif1p binds **DNA** in vitro and, through in vivo crosslinking and chromatin immuno pptn. assays, demonstrate that it targets Lig4p to chromosomal **DNA** double-strand breaks. Furthermore, this targeting requires another key NHEJ protein, **Ku**.
RE.CNT 18
RE
(1) Bliss, T; J Biol Chem 1997, V272, P5765 HCAPLUS
(2) Bryans, M; Mut Res DNA Repair 1999, V433, P53 HCAPLUS
(3) Callebaut, I; FEBS Lett 1997, V400, P25 HCAPLUS
(4) Grawunder, U; Curr Biol 1998, V8, P873 HCAPLUS
(5) Grawunder, U; Nature 1997, V388, P492 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:437961 HCAPLUS
DN 131:197758
TI Identification of a defect in **DNA ligase IV** in a radiosensitive leukaemia patient
AU Riballo, E.; **Critchlow, S. E.**; Teo, S-H.; Doherty, A. J.; Priestley, A.; Broughton, B.; Kysela, B.; Beamish, H.; Plowman, N.; Arlett, C. F.; Lehmann, A. R.; **Jackson, S. P.**; Jeggo, P. A.
CS MRC Cell Mutation Unit, University of Sussex, Brighton, BN1 9RR, UK
SO Curr. Biol. (1999), 9(13), 699-702
CODEN: CUBLE2; ISSN: 0960-9822
PB Current Biology Publications
DT Journal
LA English
AB The major mechanisms for the repair of **DNA** double-strand breaks (DSBs) in mammalian cells is non-homologous end-joining (NHEJ), a process that involves the **DNA**-dependent protein kinase, **XRCC4** and **DNA ligase IV**. Rodent cells and mice defective in these components are radiation-sensitive and defective in V(D)J-recombination, showing that NHEJ also functions to rejoin DSBs introduced during lymphocyte development. 180BR is a radiosensitive cell line defective in DSB repair, which was derived from a leukemia patient who was highly sensitive to radiotherapy. The authors have identified a mutation within a highly conserved motif encompassing the active site in **DNA ligase IV** from 180BR cells. The mutated protein is severely compromised in its ability to form a stable enzyme-adenylate complex, although residual activity can be detected at high ATP concns. The authors' results characterize the first patient with a defect in an NHEJ component and suggest that a significant defect in NHEJ that leads to pronounced radiosensitivity is compatible with normal human viability and does not cause any major immune dysfunction. The defect, however, may confer a predisposition to leukemia.

IT **9015-85-4, DNA ligase IV**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**DNA ligase IV** active site defect in human cell line from radiosensitive leukemia patient and compromised ability to form stable enzyme-adenylate complex and catalyze non-homologous end-joining)

RE.CNT 21
RE
(1) Badie, C; Cancer Res 1995, V55, P1232 HCAPLUS
(2) Badie, C; Cancer Res 1997, V57, P4600 HCAPLUS
(3) Barnes, D; Curr Biol 1998, V8, P1395 HCAPLUS
(4) Critchlow, S; Curr Biol 1997, V7, P588 HCAPLUS
(5) Critchlow, S; Trends Biochem Sci 1998, V23, P394 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:590687 HCAPLUS
DN 129:227493
TI Telomerase activity **assays**
IN Harley, Calvin Bruce; Kim, Nam Woo; Weinrich, Scott Lawrence
PA Geron Corp., USA
SO U.S., 35 pp. Cont.-in-part of U.S. Ser. No. 482,132.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 20

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5804380	A	19980908	US 1996-632662	19960415	<--
	US 5645986	A	19970708	US 1993-153051	19931112	<--
	US 5830644	A	19981103	US 1993-151477	19931112	<--
	US 5989807	A	19991123	US 1994-255774	19940607	<--
	US 5629154	A	19970513	US 1994-315214	19940928	<--
	US 5837453	A	19981117	US 1995-482132	19950607	<--
	WO 9715687	A1	19970501	WO 1996-US9669	19960607	<--
	W: AU, CA, JP, US					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	JP 11507839	T2	19990713	JP 1996-512229	19960607	<--
	AU 9663808	A1	19970515	AU 1996-63808	19960610	<--

PRAI	US 1993-151477	19931112	<--
	US 1993-153051	19931112	<--
	US 1994-255774	19940607	<--
	US 1994-315214	19940928	<--
	US 1995-482132	19950607	<--
	US 1992-882438	19920513	<--
	US 1993-38766	19930324	<--
	US 1993-60952	19930513	<--
	US 1996-631554	19960412	<--
	US 1996-632662	19960415	<--
	WO 1996-US9669	19960607	<--

AB Telomerase activity in a sample can be measured using a two reaction protocol. The first reaction involves the formation of telomerase substrate extension products from a telomerase substrate. The second reaction involves replication of the telomerase substrate extension products and/or amplification of signal generated by a bound probe. The presence of telomerase activity in a human somatic tissue or cell sample is pos. correlated with the presence of cancer and can be used to diagnose a disease or other conditions of medical interest, as well as the course of disease progression or remission in a patient. It is an object of this invention to provide a readily reproducible assay system for detecting telomerase activity, which is simple enough to use in the smaller (or low budget) clin. setting, but has the potential for high throughput using readily available robotics technol.

IT **9012-90-2**, DNA polymerase **9015-85-4, DNA**

ligase
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(telomerase activity assays)

L84 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:493734 HCAPLUS
DN 129:118798
TI The yeast homolog of **DNA ligase IV**, and the role of the enzyme in **Ku**-associated **DNA repair**
IN **Jackson, Stephen Philip; Critchlow, Susan Elizabeth**
PA Cancer Research Campaign Technology Ltd., UK; Jackson, Stephen Philip; Critchlow, Susan Elizabeth
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9830902	A1	19980716	WO 1998-GB95	19980113 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855681	A1	19980803	AU 1998-55681	19980113 <--
GB 2322193	A1	19980819	GB 1998-663	19980113 <--
GB 2322193	B2	19990929		
GB 2329248	A1	19990317	GB 1998-20952	19980113 <--
GB 2329248	B2	19990922		
GB 2329469	A1	19990324	GB 1998-20948	19980113 <--
GB 2329469	B2	19990922		
EP 966683	A1	19991229	EP 1998-900589	19980113 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI GB 1997-574 19970113 <--
GB 1997-13131 19970620
GB 1998-663 19980113
WO 1998-GB95 19980113

AB A yeast homolog of mammalian **DNA ligase IV** is provided and a role for **DNA ligase IV** established in the **Ku**-assocd. **DNA** repair (KADR) pathway. Interactions between **DNA ligase IV** and **XRCC4**, and interaction between **XRCC4** and **DNA-PKcs/Ku** are established. These interactions may be targets for modulators of **DNA** repair useful in the treatment of cancers, retroviral infections, immune system disorders and other conditions in which cellular **DNA** repair activity plays a role. Individuals with a predisposition to a disorder in which **DNA** repair plays a role may be diagnosed, by screening for the presence or absence of a defect in **XRCC4** and/or **DNA ligase IV** activity.

IT **9015-85-4, DNA ligase**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**IV**; yeast homolog of **DNA ligase IV**, and role of enzyme in **Ku**-assocd. **DNA** repair)

IT **172493-00-4D**, Protein (human clone c734 gene **XRCC4**), fragments **210229-10-0 210229-11-1**
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses)
(in modulation of protein interactions in **DNA** repair; yeast homolog of **DNA ligase IV**, and role of enzyme in **Ku**-assocd. **DNA** repair)

IT **195215-93-1**
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(yeast homolog of **DNA ligase IV**, and role of enzyme in **Ku**-assocd. **DNA** repair)

L84 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:465357 HCAPLUS
DN 129:199647
TI DNA ligase IV binds to XRCC4 via a motif located between rather than within its BRCT domains
AU Grawunder, Ulf; Zimmer, David; Lieber, Michael R.
CS Univ. Southern California Sch. Med., Norris Comprehensive Cancer Center, Depts. Pathology, Biochemistry and Molecular Biology, and Molecular Microbiology and Immunology, Los Angeles, CA, 90033, USA
SO Curr. Biol. (1998), 8(15), 873-876
CODEN: CUBLE2; ISSN: 0960-9822
PB Current Biology Ltd.
DT Journal
LA English
AB The covalent rejoining of DNA ends at single-stranded or double-stranded DNA breaks is catalyzed by DNA ligases. Four DNA ligase activities (I-IV) have been identified in mammalian cells. It has recently been demonstrated that DNA ligase IV interacts with and is catalytically stimulated by the XRCC4 protein, which is essential for DNA double-strand break repair and the genomic rearrangement process of V(D)J recombination. Together with the finding that the yeast DNA ligase IV homolog is essential for non-homologous DNA end joining, this has led to the hypothesis that mammalian DNA ligase IV catalyzes ligation steps in both of these processes. DNA ligase IV is characterized by a unique carboxy-terminal tail comprising two BRCT (BRCA1 carboxyl terminus) domains. BRCT domains were initially identified in the breast cancer susceptibility protein BRCA1, but are also found in other DNA repair proteins. It has been suggested that DNA ligase IV assocs. with XRCC4 via its tandem BRCT domains and that this may be a general model for protein-protein interactions between DNA repair proteins. We have performed a detailed deletional anal. of DNA ligase IV to define its XRC4-binding domain and to characterize regions essential for its catalytic activity. We find that a region in the carboxy-terminal tail of DNA ligase IV located between rather than within BRCT domains is necessary and sufficient to coner binding to XRCC4. The catalytic activity of DNA ligase IV is affected by mutations within the first two-thirds of the protein including a 67 amino-acid amino-terminal region that was previously thought not to be present in human DNA ligase IV.
IT **212133-68-1**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; DNA ligase IV binds to XRCC4 via a motif located between rather than within its BRCT domains)

L84 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:396022 HCAPLUS
DN 129:134723
TI Fanconi anemia C gene product plays a role in the fidelity of blunt DNA end-joining
AU Escarceller, M.; Buchwald, M.; Singleton, B. K.; Jeggo, P. A.; **Jackson, S. P.**; Moustacchi, E.; Papadopoulo, D.
CS UMR 218 CNRS LRC n.degree.1 du CEA Institut Curie-Recherche, Paris, 75248, Fr.
SO J. Mol. Biol. (1998), 279(2), 375-385
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press Ltd.

DT Journal
LA English
AB Mutations in genes controlling the correct functioning of the replicative, repair and recombination machineries may lead to genomic instability. A high level of spontaneous chromosomal aberrations amplified by treatment with DNA crosslinking agents is the hallmark of Fanconi anemia (FA), an inherited chromosomal instability syndrome assocd. with cancer proneness. Two of the eight FA genes have been cloned (FAA and FAC), but their function has not yet been defined. The lack of homol. with known genes suggests the involvement of FA genes in a novel pathway specific to vertebrates. Using a DNA end-joining assay in cultured cells, we studied the processing of both blunt and cohesive-ended double strand breaks (DSB) in normal and FA cells. The results show that: (i) the overall ligation efficiency is normal in FA lymphoblasts; (ii) in FA-C, error-free processing of blunt-ended DSB is markedly decreased, resulting in a higher deletion frequency and larger deletion size; (iii) the fidelity of processing of blunt-DSB is completely restored in FACC cells (complemented with wild-type FAC gene) and the deletion size shifted to values similar to that obsd. in normal cells; (i.v.) the fidelity of cohesive end-joining is not affected in FA cells; (v) activities and/or expression of known factors involved in DSB processing, such as the components of the DNA-**PK** complex and **XRCC4**, are normal in FA cells. Our results provide strong evidence that the lack of a functional FAC gene results in loss of fidelity of end-joining, which likely accounts for the FA-C phenotype of chromosome instability. We conclude that FAC, and perhaps all FA gene products, are likely to play a role in the fidelity of end-joining of specific DSB.

L84 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:692922 HCAPLUS
DN 128:2812
TI Molecular genetic characterization of **XRCC4** function
AU Mizuta, Ryushi; Cheng, Hwei-Ling; Gao, Yijie; Alt, Frederick W.
CS Children's Hosp., Dep. Genetics, Harvard Medical School, Howard Hughes Medical Inst., Boston, MA, 02115, USA
SO Int. Immunol. (**1997**), 9(10), 1607-1613
CODEN: INIMEN; ISSN: 0953-8178
PB Oxford University Press
DT Journal
LA English
AB **XRCC4** is a generally expressed protein of 334 amino acids that is involved in the repair of DNA double-stranded breaks and in V(D)J recombination, but its function is unknown. In this study, we have used a mutational approach and the yeast two-hybrid method to perform an initial characterization of this protein. We show that the **XRCC4** protein is located in the nucleus. We also demonstrate that several potential phosphorylation sites are not required for **XRCC4** function in a transient V(D)J recombination assay. In addn., we show that **XRCC4** forms a homodimer in vivo with the homodimerization domain being located within amino acids 115-204. Finally, we define a core domain of **XRCC4** that functions in V(D)J recombination and comprises amino acids 18-204. Potential functions of **XRCC4** are discussed.

L84 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:662836 HCAPLUS
DN 127:258612
TI V(D)J recombination and double strand break repair: biochemical analysis of DNA-**pkcs** and **XRCC4** (immune deficiency)
AU Leber, Ray Allen
CS Southwestern Medical Center, Univ. of Texas, Dallas, TX, USA
SO (**1997**) 1698 pp. Avail.: UMI, Order No. DA0598089
From: Diss. Abstr. Int., B 1997, 58(4), 1698
DT Dissertation
LA English
AB Unavailable

L84 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:544642 HCAPLUS
DN 127:244613
TI Identification of Saccharomyces cerevisiae **DNA ligase IV**: involvement in **DNA** double-strand break repair
AU Teo, Soo-Hwang; **Jackson, Stephen P.**
CS Wellcome/CRC Institute and Department of Zoology, University of Cambridge, Cambridge, CB2 1QR, UK
SO EMBO J. (**1997**), 16(15), 4788-4795
CODEN: EMJODG; ISSN: 0261-4189
PB Oxford University Press
DT Journal
LA English
AB **DNA ligases** catalyze the joining of single and double-strand **DNA** breaks, which is an essential final step in **DNA** replication, recombination and repair. Mammalian cells have four **DNA ligases**, termed **ligases** I-**IV**. In contrast, other than a **DNA ligase** I homolog (encoded by CDC9), no other **DNA ligases** have hitherto been identified in Saccharomyces cerevisiae. Here, we report the identification and characterization of a novel gene, LIG4, which encodes a protein with strong homol. to mammalian **DNA ligase IV**. Unlike CDC9, LIG4 is not essential for **DNA** replication, RAD52-dependent homologous recombination nor the repair of UV light-induced **DNA** damage. Instead, it encodes a crucial component of the non-homologous end-joining (NHEJ) app., which repairs **DNA** double-strand breaks that are generated by ionizing radiation or restriction enzyme digestion: a function which cannot be complemented by CDC9. Lig4p acts in the same **DNA** repair pathway as the **DNA** end-binding protein **Ku**. However, unlike **Ku**, it does not function in telomere length homeostasis. These findings indicate diversification of function between different eukaryotic **DNA ligases**. Furthermore, they provide insights into mechanisms of **DNA** repair and suggest that the NHEJ pathway is highly conserved throughout the eukaryotic kingdom.
IT **9015-85-4, DNA ligase**
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(**IV**; identification of Saccharomyces cerevisiae **DNA ligase IV**: involvement in **DNA** double-strand break repair)
IT **195215-93-1**
RL: PRP (Properties)
(amino acid sequence; identification of Saccharomyces cerevisiae **DNA ligase IV**: involvement in **DNA** double-strand break repair)

L84 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:532832 HCAPLUS
DN 127:243926
TI Mammalian **DNA** double-strand break repair protein **XRCC4** interacts with **DNA ligase IV**
AU **Critchlow, Susan E.**; Bowater, Richard P.; **Jackson, Stephen P.**
CS Wellcome/CRC Inst., Cambridge, CB2 1QR, UK
SO Curr. Biol. (**1997**), 7(8), 588-598
CODEN: CUBLE2; ISSN: 0960-9822
PB Current Biology
DT Journal
LA English
AB Background: Mammalian Cells deficient in the **XRCC4 DNA** repair protein are impaired in **DNA** double-strand break repair and are consequently hypersensitive to ionizing radiation. These cells are also defective in site-specific V(D)J recombination, a process that generates the diversity of antigen receptor genes in the developing immune

system. These features are shared by cells lacking components of the **DNA**-dependent protein kinase (**DNA-PK**). Although the **XRCC4** gene has been cloned, the function(s) of **XRCC4** in **DNA** end-joining has remained elusive. Results: We found the XRCCR is a nuclear phosphoprotein and was an effective substrate in vitro for **DNA-PK**. Human **XRCC4** assocd. extremely tightly with another protein(s) even in the presence of 1 M NaCl. Co-immunopptn. and adenylylation assays demonstrated that this assocd. factor was the recently identified human **DNA ligase IV**. Consistent with this, **XRCC4** and **DNA ligase IV** copurified exclusively and virtually quant. over a variety of chromatog. steps. Protein mapping studies revealed that **XRCC4** interacted with **ligase IV** via the unique carboxy-terminal **ligase IV** extension that comprises two tandem BRCT (BRCA1 carboxyl terminus) homol. motifs, which are also found in other **DNA** repair-assocd. factors and in the breast cancer susceptibility protein BRCA1. Conclusions: Our findings provide a function for the carboxy-terminal region of **ligase IV** and suggest that BRCT domains of other proteins may mediate contacts between **DNA** repair components. In addn., our data implicate mammalian **ligase IV** in V(D)J recombination and the repair of radiation-induced **DNA** damage, and provide a model for the potentiation of these processes by **XRCC4**.

IT **9015-85-4, DNA ligase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(**IV**; mammalian **DNA** double-strand break repair protein **XRCC4** interacts with **DNA ligase IV**)

L84 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:516020 HCAPLUS
DN 127:230262
TI Yeast DNA ligase IV mediates non-homologous DNA end joining
AU Wilson, Thomas E.; Grawunder, Ulf; Lieber, Michael R.
CS Div. of Lab. Med., Washington Univ. Sch. of Med., St. Louis, MO, 63110, USA
SO Nature (London) (1997), 388(6641), 495-498
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
AB The discovery of homologs from the yeast Saccharomyces cerevisiae of the human Ku DNA-end-binding proteins (HDF1 and KU80) has established that this organism is capable of nonhomologous double-strand end joining (NHEJ), a form of DNA double-strand break repair (DSBR) active in mammalian V(D)J recombination. Identification of the DNA ligase that mediates NHEJ in yeast will help elucidate the function of the 4 mammalian DNA ligases in DSBR, V(D)J recombination and other reactions. Here, it is shown that S. cerevisiae has 2 typical DNA ligases, the known DNA ligase I homolog CDC9 and the previously unknown DNA ligase IV homolog DNL4. Dnl4 mutants are deficient in precise and end-processed NHEJ. DNL4 and HDF1 are epistatic in this regard, with the mutation of each having equiv. effects. Dnl4 mutants are complemented by overexpression of Dnl4 but not a Cdc9, and deficiency of Dnl4 alone does not impair either cell growth or the Cdc9-mediated responses to ionizing and UV radiation. Thus, . cerevisiae has 2 distinct and sep. ligation pathways.

IT **195215-93-1**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(amino acid sequence; yeast DNA ligase IV mediates non-homologous DNA end joining)

L84 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:516010 HCAPLUS
DN 127:231068
TI Activity of **DNA ligase IV** stimulated by complex formation with **XRCC4** protein in mammalian cells
AU Grawunder, Ulf; Wilm, Matthias; Wu, Xiantuo; Kulesza, Peter; Wilson, Thomas E.; Mann, Matthias; Lieber, Michael R.
CS Div. of Mol. Oncol., Dep. of Pathol., Washington Univ. Sch. of Med., St. Louis, MO, 63110, USA
SO Nature (London) (**1997**), 388(6641), 492-495
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
AB Mutation of the **XRCC4** gene in mammalian cells prevents the formation of the signal and coding joints in the V(D)J recombination reaction, which is necessary for prodn. of a functional Ig gene, and renders the cells highly sensitive to ionizing radiation. However, **XRCC4** shares no sequence homol. with other proteins, nor does it have a biochem. activity to indicate what its function might be. Here, it is shown that **DNA ligase IV** co-immunoppts. with **XRCC4** and that these 2 proteins specifically interact with one another in a yeast 2-hybrid system. Ligation of **DNA** double-strand breaks in a cell-free system by **DNA ligase IV** is increased 5-fold by purified **XRCC4** and 7-8-fold when **XRCC4** is co-expressed with **DNA ligase IV**. Thus, the biol. consequences of mutating **XRCC4** are primarily due to the loss of its stimulatory effect on **DNA ligase IV**: the function of the **XRCC4**-**DNA ligase IV** complex may be to carry out the final steps of V(D)J recombination and joining of **DNA** ends.
IT **9015-85-4, DNA ligase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**IV**; activity of **DNA ligase IV** stimulated by complex formation with **XRCC4** protein in mammalian cells)

L84 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:479550 HCAPLUS
DN 127:204133
TI **Ku70**-deficient embryonic stem cells have increased ionizing radiosensitivity, defective DNA end-binding activity, and inability to support V(D)J recombination
AU Gu, Yansong; Jin, Shengfang; Gao, Yijie; Weaver, David T.; Alt, Frederick W.
CS Children's Hospital, Harvard Medical School, Boston, MA, 02115, USA
SO Proc. Natl. Acad. Sci. U. S. A. (**1997**), 94(15), 8076-8081
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB V(D)J recombination requires both lymphoid-specific and generally expressed enzymic activities. All three known generally expressed activities involved in V(D)J recombination are also involved in DNA double-strand break repair (DSBR). Two of these are components of the DNA-dependent protein kinase (DNA-**PK**) and include **Ku80** and DNA-**PK** catalytic subunit (DNA-**PKcs**); the third, **XRCC4**, is a protein of unknown function. The **Ku70** protein is an addnl. component of DNA-**PK**; **Ku70** forms a heterodimer with **Ku80** to generate the DNA end-binding component of the enzyme. To test putative functions for **Ku70**, we have used gene-targeted mutation to generate a murine embryonic stem cell line which lacks **Ku70** expression. We find that the **Ku70**-/- cells produce no detectable **Ku70** and very little **Ku80**, suggesting a direct interrelationship between their levels. Correspondingly, these cells lack the nonspecific DNA end-binding activity assocd. with **Ku**. Significantly, the **Ku70**-/- embryonic

stem cells have markedly increased sensitivity to .gamma.-irradn. relative to **Ku70**+/- or wild-type embryonic stem cells. Furthermore, the **Ku70**-/- cells lack the ability to effectively rejoin signal and coding ends liberated in transiently introduced V(D)J recombination substrates by enforced RAG-1 and RAG-2 expression. We conclude that the **Ku70** gene product is involved in DSBR and V(D)J recombination and confirm that the **Ku70** gene can be classified as a member of the x-ray cross-complementation group 6 (XRCC6). Potential differences between the **Ku70**-/- and **Ku80**-/- V(D)J recombination defects are discussed.

L84 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:446105 HCAPLUS
DN 127:104843
TI The end-joining reaction in V(D)J recombination
AU Smider, Vaughn; Chu, Gilbert
CS Departments of Medicine and Biochemistry, Stanford University Medical Center, Stanford, CA, 94305, USA
SO Semin. Immunol. (**1997**), 9(3), 189-197
CODEN: SEIME2; ISSN: 1044-5323
PB Academic
DT Journal; General Review
LA English
AB A review with 76 refs. V(D)J recombination consists of a DNA cleavage reaction catalyzed by RAG1 and RAG2, followed by an end-joining reaction that utilizes the cell's double-strand break repair machinery. Genes essential for the end-joining reaction include: **XRCC4** encoding a protein of unknown enzymic function; XRCC5 and XRCC6 encoding 86 and 70 kDa subunits of the **Ku** autoantigen, a DNA end-binding protein that is also the regulatory subunit of DNA-dependent protein kinase (DNA-**PK**); and XRCC7 encoding the catalytic subunit (DNA-**PKcs**) of DNA-**PK**. Recent progress in understanding the cleavage reaction, coupled with what was previously known about **Ku**, DNA-**PK**, and double-strand break repair, provide the foundation for a working model of how V(D)J recombination might be catalyzed.

L84 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:163835 HCAPLUS
TI Dna dendrimers: Assembly and signal amplification
AU Vogelbacker, Helen H.; Getts, Robert C.; Tian, Nian; Labaczewski, Robert; Nilsen, Thor W.
CS Polyprobe Inc., Bala Cynwyd, PA, 19004, USA
SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (**1997**), PMSE-278 Publisher: American Chemical Society, Washington, D. C.
CODEN: 64AOAA
DT Conference; Meeting Abstract
LA English
AB Nucleic acid blots are the method of choice for genetic diagnosis, forensic identification and detn. of parentage. DNA dendrimers provide an excellent method for amplifying signal in nucleic acid assays. We have developed and assembled dendritic DNA with hundreds to thousands of single stranded binding sites. Specificity to a particular target sequence is conferred to dendrimers by hybridizing and covalently crosslinking oligonucleotides to the outer surface of the dendrimers. Addn. of DNA dendrimers in conventional nucleic acid blot assays results in signal amplification greater than 100-fold compared to oligonucleotides alone. DNA dendrimers with specificity to seven different DNA sequences have been used to amplify signal(s) in DNA blots. We have constructed DNA dendrimers with specificity to HIV1 LTR, .beta.2-microglobulin, FSHr (FSH receptor) and **XRCC4** (X-ray repair) sequences and utilized these dendrimers in conventional Southern and dot blot assays. Southern blots probed with DNA dendrimers having 50 bases of sequence specificity to FSHr and 32P-labeled oligonucleotides have identified the same bands in human genomic digests as a traditionally labeled 700bp cDNA probe. Amplification of signal by dendrimers occurs independent of the label used

in the assay. 32P, digoxigenin, biotin and alk. phosphatase labeled probes all yield signal enhancement when used with DNA dendrimers.

L84 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:143120 HCAPLUS
DN 126:221089
TI Tying loose ends: roles of **Ku** and DNA-dependent protein kinase in the repair of double-strand breaks
AU Lieber, Michael R.; Grawunder, Ulf; Wu, Xiantuo; Yaneva, Mariana
CS Division of Molecular Oncology, Department of Pathology, Biochemistry and Molecular Biophysics, St. Louis, MO, 63110, USA
SO Curr. Opin. Genet. Dev. (**1997**), 7(1), 99-104
CODEN: COGDET; ISSN: 0959-437X
PB Current Biology
DT Journal; General Review
LA English
AB A review with 68 refs. A convergence of information from biochem., yeast and mammalian genetics, immunol., and radiation biol. has permitted identification of some of the protein participants - **Ku**, DNA-**PK**, **XRCC4** - and the reaction intermediates in DNA end joining, suggesting how broken chromosomal ends may be recognized and repaired in eukaryotic cells. Some components may be inherited disorders.

L84 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:670559 HCAPLUS
DN 125:319694
TI The **XRCC4** gene encodes a novel protein involved in DNA double-strand break repair and V(D)J recombination (DNA repair)
AU Li, Zhiying
CS Harvard Univ., Cambridge, MA, USA
SO (**1996**) 76 pp. Avail.: Univ. Microfilms Int., Order No. DA9631541
From: Diss. Abstr. Int., B 1996, 57(6), 3576
DT Dissertation
LA English
AB Unavailable

L84 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:593076 HCAPLUS
DN 125:239401
TI Identification of the **XRCC4** gene: complementation of the DSBR and V(D)J recombination defects of XR-1 cells
AU Li, Zhiying; Alt, Frederick W.
CS Center for Blood Research, Harvard Medical School, Boston, MA, 02115, USA
SO Curr. Top. Microbiol. Immunol. (**1996**), 217(Molecular Analysis of DNA Rearrangements in the Immune System), 143-150
CODEN: CTMIA3; ISSN: 0070-217X
DT Journal; General Review
LA English
AB A review with 27 refs. on the identification of the human gene **XRCC4**, which can complement the XR-1 defects and which maps to human chromosome 5. XR-1 cells are very radiosensitive and defective in V(D)J recombination. Topics discussed include complementation cloning of **XRCC4**, characterization of the gene, and potential functions of the encoded protein.

L84 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:458126 HCAPLUS
DN 125:107046
TI Nucleic acid library arrays, methods for synthesizing them and methods for sequencing and sample **screening** using them
IN Lockhart, David J.; Chee, Mark S.; Vetter, Dirk; Diggelmann, Martin
PA Affymax Technologies N.V., Neth. Antilles
SO Eur. Pat. Appl., 73 pp.
CODEN: EPXXDW
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 721016	A2	19960710	EP 1995-307501	19951020 <--
	EP 721016	A3	19991103		
	R: DE, FR, GB, IT, NL				
	US 5556752	A	19960917	US 1994-327687	19941024 <--
	US 5770722	A	19980623	US 1996-664093	19960613 <--
PRAI	US 1994-327522	19941021 <--			
	US 1994-327687	19941024 <--			
	US 1995-533582	19951018 <--			

AB Disclosed are methods for discriminating between fully complementary hybrids and those that differ by one or more base pairs and libraries of unimol., double-stranded oligonucleotides on a solid support. In these methods, the quality of hybridization signals on high d. oligonucleotide arrays is improved by (1) the nuclease treatment and (2) ligation reactions. Also provided are libraries of unimol. or intermol., double-stranded oligonucleotides on a solid support. These libraries are useful in pharmaceutical discovery for the **screening** of numerous biol. samples for specific interactions between the double-stranded oligonucleotides, and peptides, proteins, **drugs** and RNA. In a related aspect, the present invention provides libraries of conformationally restricted probes on a solid support. The probes are restricted in their movement and flexibility using double-stranded oligonucleotides as scaffolding. The probes are also useful in various **screening** procedures assocd. with **drug** discovery and diagnosis. The present invention further provides methods for the prepn. and screening of the above libraries.

IT **9015-85-4, DNA ligase**
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleic acid library arrays, methods for synthesizing them and methods for sequencing and sample screening using them)

L84 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:416784 HCAPLUS
TI Bisimidazoacridone binding to nucleic acids: Thermodynamic, kinetic, spectroscopic, and electrophoretic mobility studies.
AU Bansal, M.; Casas-Finet, J.; Cholody, W. M.; Michejda, C. J.
CS Molecular Aspects Drug Design, ABL-BRP, Frederick, MD, 21702, USA
SO Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29 (**1996**), TOXI-023 Publisher: American Chemical Society, Washington, D. C.
CODEN: 63BFAF
DT Conference; Meeting Abstract
LA English
AB WMC-26, a bisimidazoacridone (BIA), shows promise as a selective antitumor agent against colon cancer in the NCI in vitro screen and exhibits nanomolar range toxicity in colony survival assays. This compd. binds **DNA** in vitro, decreases the level of transcription in cells, and exhibits only moderate cytotoxicity to repair-deficient cell lines suggesting **DNA** as the primary cellular target. Thus, understanding **DNA** binding and kinetics is integral to rational **drug design**. Using a **ligase** assay to monitor BIA intercalation, we showed that WMC-26, as well as other BIAs, were bound to **DNA** at least in a monointercalated structure in agreement with gel shift assays employing supercoiled SV40 **DNA**. We have investigated the thermodn. and kinetics of binding to nucleic acids using WMC-26 as the prototype compd. Stopped-flow kinetic traces fit a bi-exponential function. Dissocn. reactions were found to be significantly slower than assocn. reactions, and the kinetics depended on the type of nucleic acid polymer used. Our results of BIA binding to nucleic acids of various structure (rRNA, **DNA**-RNA hybrids, ss and ds **DNA**) and sequence (GC vs. AT) suggest a preliminary

binding model. Research sponsored by the National Cancer Institute, DHHS, under contract with ABL.

L84 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:202262 HCAPLUS
DN 124:280620
TI Complementation mapping in microcell hybrids: localization of **XRCC4** to 5q15-q21
AU Athwal, Raghbir S.; Kaur, Gursurinder P.
CS Dep. Pathology, Temple Univ. School Medicine, Philadelphia, PA, 19140, USA
SO Methods (San Diego) (**1996**), 9(1), 12-19
CODEN: MTHDE9; ISSN: 1046-2023
DT Journal
LA English
AB Microcell-mediated chromosome transfer (MMCT) offers a unique method for introducing tagged individual human chromosomes from mouse/human monochromosomal hybrids into cell lines of displaying recessive mutant phenotypes. Functional anal. of the resultant microcell hybrids bearing different tagged individual human chromosomes permits identification of the complementing chromosome. Using this approach, a no. of human DNA repair genes that complement DNA repair defects in xeroderma pigmentosum, ataxia telangiectasia, Bloom's syndrome, and rodent mutant cells have been mapped to specific chromosomes. This paper presents expts. performed to map a DNA double-strand break (dsb) repair gene, **XRCC4**, to human chromosome 5q15-q21. The introduction of human chromosome 5 into Chinese hamster mutant XR-1 cells cor. their x-ray sensitivity and DNA dsb repair deficiency. Loss of chromosome 5 and concomitant reversion to the radiosensitive phenotype confirmed the presence of **XRCC4** on this chromosome. Anal. of DNA markers in radiation-resistant and -sensitive clones bearing different segments of chromosome 5 placed this gene in the region 5q15-q21. These studies demonstrate the application of MMCT technol. to the genetic anal. of mutations that escape other exptl. approaches.

L84 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:14738 HCAPLUS
DN 124:84398
TI The **XRCC4** gene encodes a novel protein involved in DNA double-strand break repair and V(D)J recombination
AU Li, Zhiying; Otevrel, Tomas; Gao, Yijie; Cheng, Hwei-Ling; Seed, Brian; Stamato, Thomas D.; Taccioli, Guillermo E.; Alt, Frederick W.
CS Cent. Blood Res., Harvard Univ. Med. Sch., Boston, MA, 02115, USA
SO Cell (Cambridge, Mass.) (**1995**), 83(7), 1079-89
CODEN: CELLB5; ISSN: 0092-8674
DT Journal
LA English
AB The XR-1 Chinese hamster ovary cell line is impaired in DNA double-strand break repair (DSBR) and in ability to support V(D)J recombination of transiently introduced substrates. The authors now show that XR-1 cells support recombination-activating gene 1- and 2-mediated initiation of V(D)J recombination within a chromosomally integrated substrate, but are highly impaired in ability to complete the process by forming coding and recognition sequence joins. On this basis, the authors isolated a human cDNA sequence, termed **XRCC4**, whose expression confers normal V(D)J recombination ability and significant restoration of DSBR activity to XR-1, clearly demonstrating that this gene product is involved in both processes. The **XRCC4** gene maps to the previously identified locus on human chromosome 5, is deleted in XR-1 cells, and encodes a ubiquitously expressed product unrelated to any described protein.
IT **172493-00-4**, Protein (human clone c734 gene **XRCC4**)
RL: PRP (Properties)
(amino acid sequence; human **XRCC4** gene encodes protein involved in DNA double-strand break repair and V(D)J recombination)
IT **172726-41-9**, Protein (mouse gene **Xrcc4**)
RL: PRP (Properties)
(amino acid sequence; sequence of mouse **Xrcc4** protein

involved in DNA double-strand break repair and V(D)J recombination)

IT **172444-63-2**
RL: PRP (Properties)
(nucleotide sequence; human **XRCC4** gene encodes protein involved in DNA double-strand break repair and V(D)J recombination)

L84 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:814858 HCAPLUS
DN 123:247718
TI Nomenclature of human genes involved in ionizing radiation sensitivity
AU Thompson, Larry H.; Jeggo, Penny A.
CS Biology and Biotechnology Research Program, L452, Lawrence Livermore National Laboratory, P.O. Box 808, Livermore, CA, 94551-0808, USA
SO Mutat. Res. (**1995**), 337(2), 131-4
CODEN: MUREAV; ISSN: 0027-5107
DT Journal; General Review
LA English
AB A review with 34 refs. As the human genes involved in cellular response to ionizing radiation are being mapped and cloned at an increasing pace, it is important to establish uniformity of nomenclature. To date they are: gene XRCC1 on chromosome 19q13.2-q13.3, gene XRCC2 on chromosome 7q36, gene XRCC3 on chromosome 14q32.3, gene **XRCC4** on chromosome 5q13-q14, gene XRCC5/**Ku86** on chromosome 2q34-36, gene XRCC6/**Ku70** on chromosome 22q13, gene XRCC7/SCID/DNA-**PKcs** on chromosome 8p11.1-q11.1.

L84 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:607962 HCAPLUS
DN 123:27211
TI Rapid mutational analysis method for mapping protein binding sites for monoclonal antibodies or other ligands and potential use in **drug design**
IN Seed, Brian; Peterson, Andrew
PA The General Hospital Corporation, USA
SO U.S., 28 pp. Cont.-in-part of U.S. Ser. No. 181,826, abndoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5411861	A	19950502	US 1992-842465	19920227 <--
	DK 8901725	A	19891212	DK 1989-1725	19890411 <--
	DK 172110	B1	19971027		
	ES 2065933	T3	19950301	ES 1989-106627	19890413 <--
	JP 02203787	A2	19900813	JP 1989-96191	19890414 <--
	US 5955264	A	19990921	US 1994-320663	19941011 <--
PRAI	US 1988-181826	19880415 <--			
	US 1992-842465	19920227 <--			

AB A novel rapid mutational anal. method for mapping protein epitopes is disclosed. This method has been used to identify the binding sites for 16 anti-CD2 and anti-CD4 monoclonal antibodies. The powerful, rapid, and simple method of the present invention allows isolation of a very large no. of mutants, and is applicable to any intracellular or surface protein for which a cDNA and monoclonal antibodies are available. The present method is esp. useful in ligand binding site studies for the **design** of new ligands and **drugs**.
IT **9012-90-2**, DNA polymerase **9015-85-4**, **DNA ligase**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(rapid mutational anal. method for mapping protein binding sites for monoclonal antibodies or other ligands and potential use in **drug design**)

L84 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:582229 HCAPLUS
DN 123:26967
TI Regional localization of the **XRCC4** human radiation repair gene
AU Otevrel, Tomas; Stamato, Thomas D.
CS Lankenau Med. Res. Center, Wynnewood, PA, 19151, USA
SO Genomics (**1995**), 27(1), 211-14
CODEN: GNMCEP; ISSN: 0888-7543
DT Journal
LA English
AB To map the **XRCC4** human DNA repair gene subchromosomally, a gamma-ray-resistant human:XR-1 hamster hybrid cell contg. fragments of human chromosome 5 and the pSV2neo plasmid was lethally irradiated and fused with the gamma-ray-sensitive XR-1 mutant cell. After selection for G418 resistance, 2 of a total of 76 hybrids retained wildtype gamma-ray resistance. FISH anal. of normal human lymphocytes using DNA from the two resistant hybrids as probes produced a common region of hybridization of 5q13-q14, suggesting that the **XRCC4** gene is in this region of chromosome 5. The gene was phys. localized between D5S427 and D5S401 microsatellite markers and the cytol. assignment confirmed using hamster:human hybrids contg. known deletions in human chromosome 5.

L84 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:578174 HCAPLUS
DN 124:49422
TI Molecular cloning and expression of human cDNAs encoding a novel DNA ligase IV and DNA ligase III, an enzyme active in DNA repair and recombination
AU Wei, Ying-Fei; Robins, Peter; Carter, Kenneth; Caldecott, Keith; Pappin, Darryl J. C.; Yu, Guo-Liang; Wang, Rui-Ping; Shell, Brenda K.; Nash, Rachel A.; et al.
CS Human Genome Sci., Inc., Rockville, MD, 20850-3338, USA
SO Mol. Cell. Biol. (1995), 15(6), 3206-16
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB Three distinct DNA ligases, I to III, have been found previously in mammalian cells, but a cloned cDNA has been identified only for DNA ligase I, an essential enzyme active in DNA replication. A short peptide sequence conserved close to the C terminus of all known eukaryotic DNA ligases was used to search for addnl. homologous sequences in human cDNA libraries. Two different incomplete cDNA clones that showed partial homol. to the conserved peptide were identified. Full-length cDNAs were obtained and expressed by in vitro transcription and translation. The 103-kDa product of one cDNA clone formed a characteristic complex with the XRCC1 DNA repair protein and was identical with the previously described DNA ligase III. DNA ligase III appears closely related to the smaller DNA ligase II. The 96-kDa in vitro translation product of the second cDNA clone was also shown to be an ATP-dependent DNA ligase. A fourth DNA ligase (DNA ligase IV) has been purified from human cells and shown to be identical to the 96-kDa DNA ligase by unique agreement between mass spectrometry data on tryptic peptides from the purified enzyme and the predicted open reading frame of the cloned cDNA. The amino acid sequences of DNA ligases III and IV share a related active-site motif and several short regions of homol. with DNA ligase I, other DNA ligases, and RNA capping enzymes. DNA ligases III and IV are encoded by distinct genes located on human chromosomes 17q11.2-12 and 13q33-34, resp.
IT **165041-12-3**
RL: PRP (Properties)
(amino acid sequence of; mol. cloning and expression of human cDNAs encoding novel DNA ligase IV and DNA ligase III, enzyme active in DNA repair and recombination)
IT **165150-97-0**
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence of; mol. cloning and expression of human cDNAs encoding novel DNA ligase IV and DNA ligase III, enzyme active in DNA

repair and recombination)

L84 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:607557 HCAPLUS
DN 113:207557
TI Human chromosome 5 complements the DNA double-strand break-repair deficiency and gamma-ray sensitivity of the XR-I hamster variant
AU Giaccia, A. J.; Denko, N.; MacLaren, R.; Mirman, D.; Waldren, C.; Hart, I.; Stamato, T. D.
CS Wistar Inst. Anat. Biol., Philadelphia, PA, USA
SO Am. J. Hum. Genet. (**1990**), 47(3), 459-69
CODEN: AJHGAG; ISSN: 0002-9297
DT Journal
LA English
AB XR-1 is a Chinese hamster ovary (CHO) cell mutant which is unusually sensitive to killing by .gamma.-rays in the G1 portion of the cell cycle but has nearly normal resistance to .gamma.-ray damage in late S phase. This cell-cycle sensitivity correlates with the mutant's inability to repair DNA double-strand breaks (DSBs) produced by ionizing radiation and restriction enzymes. It was previously shown in somatic cell hybrids of XR-1 cells and human fibroblasts that the XR-1 mutation is a recessive mutation. In this study, using somatic cell hybrids formed between XR-1 and human fibroblasts, the human complementing gene was mapped to chromosome 5 by chromosome-segregation anal. This gene biochem. restores the hamster defect to wild-type levels of .gamma.-ray and bleomycin resistance as well as restoring its proficiency to repair DNA DSBs, suggesting that a single gene is responsible for the XR-1 phenotype. The name **XRCC4** (x-ray-complementing Chinese hamster gene 4) was assigned to this human gene until its biochem. function in repair is discovered.

=> sel hit rn l84

E9 THROUGH E19 ASSIGNED

=> fil reg

FILE 'REGISTRY' ENTERED AT 13:03:45 ON 04 JAN 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 3 JAN 2001 HIGHEST RN 312691-21-7
DICTIONARY FILE UPDATES: 3 JAN 2001 HIGHEST RN 312691-21-7

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can tot

L85 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **212133-68-1** REGISTRY
CN Synthetase, polydeoxyribonucleotide (human isoenzyme IV 911-amino acid residue isoform) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN DNA ligase IV (human)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN

SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:199647

L85 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **210229-11-1** REGISTRY
CN 728-844-Synthetase, polydeoxyribonucleotide (human isoenzyme IV) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:118798

L85 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **210229-10-0** REGISTRY
CN 591-676-Synthetase, polydeoxyribonucleotide (human isoenzyme IV) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:118798

L85 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **195215-93-1** REGISTRY
CN Synthetase, polydeoxyribonucleotide, IV (Saccharomyces cerevisiae gene DNL4) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN DNA ligase IV (Saccharomyces cerevisiae gene LIG4)
CN GenBank Z74913-derived protein GI 1420096
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:118798

REFERENCE 2: 127:244613

REFERENCE 3: 127:230262

L85 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **172726-41-9** REGISTRY
CN Protein (mouse gene Xrcc4) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:84398

L85 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **172493-00-4** REGISTRY
CN Protein (human clone c734 gene XRCC4) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:118798

REFERENCE 2: 124:84398

L85 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **172444-63-2** REGISTRY
CN DNA (human clone c734 gene XRCC4 protein cDNA plus flanks) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (human clone c734 gene XRCC4 protein messenger RNA-complementary plus 5'- and 3'-flanking region fragment)
OTHER NAMES:
CN GenBank U40622
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:84398

L85 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **165150-97-0** REGISTRY
CN DNA (human polydeoxyribonucleotide synthetase isoenzyme IV cDNA plus flanks) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (human polydeoxyribonucleotide synthetase isoenzyme IV messenger RNA-complementary plus 5'- and 3'-flanking region fragment)

OTHER NAMES:
CN GenBank X83441
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:49422

L85 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **165041-12-3** REGISTRY
CN Synthetase, polydeoxyribonucleotide (human isoenzyme IV) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:49422

L85 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **9015-85-4** REGISTRY
CN Synthetase, polydeoxyribonucleotide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ATP-dependent DNA ligase
CN Deoxyribonucleate ligase
CN Deoxyribonucleic acid joinase
CN Deoxyribonucleic acid ligase
CN Deoxyribonucleic acid repair enzyme
CN Deoxyribonucleic acid-joining enzyme
CN Deoxyribonucleic joinase
CN Deoxyribonucleic ligase
CN Deoxyribonucleic repair enzyme
CN Deoxyribonucleic-joining enzyme
CN DNA joinase
CN DNA ligase
CN DNA ligase IV
CN DNA repair enzyme
CN DNA-joining enzyme
CN E.C. 6.5.1.1
CN NHR ligase
CN Polynucleotide ligase
CN Polynucleotide synthetase
CN Polynucleotide synthetase (ATP)
CN Sealase
DR 9015-87-6, 9041-01-4
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, EMBASE, PROMT, TOXLINE, TOXLIT, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1224 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1225 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:14324

REFERENCE 2: 134:13992

REFERENCE 3: 134:13945

REFERENCE 4: 134:13937

REFERENCE 5: 134:2043

REFERENCE 6: 134:1887

REFERENCE 7: 134:1331

REFERENCE 8: 134:1109

REFERENCE 9: 133:359767

REFERENCE 10: 133:359759

L85 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN **9012-90-2** REGISTRY
CN Nucleotidyltransferase, deoxyribonucleate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN AMPLITAQ
CN Deoxyribonucleate nucleotidyltransferase
CN Deoxyribonucleate polymerase
CN Deoxyribonucleic acid duplicase
CN Deoxyribonucleic acid polymerase
CN Deoxyribonucleic duplicase
CN Deoxyribonucleic polymerase
CN Deoxyribonucleic polymerase I
CN DNA duplicase
CN DNA nucleotidyltransferase
CN DNA polymerase
CN DNA replicase
CN DNA-dependent DNA polymerase
CN DNA-directed DNA polymerase
CN Duplicase
CN E.C. 2.7.7.7
CN Sequenase
CN Taq DNA ligase
CN Taquenase
CN Thermo Sequenase
DR 9026-79-3, 9045-34-5
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, NAPRALERT, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
10583 REFERENCES IN FILE CA (1967 TO DATE)
252 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10600 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:15083

REFERENCE 2: 134:14940

REFERENCE 3: 134:14734

REFERENCE 4: 134:14696

REFERENCE 5: 134:14695

REFERENCE 6: 134:14673

REFERENCE 7: 134:14650

REFERENCE 8: 134:14647

REFERENCE 9: 134:14554

REFERENCE 10: 134:13992

=> fil biosis

FILE 'BIOSIS' ENTERED AT 13:15:53 ON 04 JAN 2001
COPYRIGHT (C) 2001 BIOSIS(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 3 January 2001 (20010103/ED)

The BIOSIS file has been reloaded. Enter HELP RLOAD and HELP REINDEXING
for details.

=> d all tot

L109 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:414608 BIOSIS
DN PREV199799706651
TI Mammalian **DNA** double-strand break repair protein **XRCC4** interacts with **DNA ligase IV**.
AU **Critchlow, Susan E.**; Bowater, Richard P.; **Jackson, Stephen P. (1)**
CS (1) Wellcome/CRC Inst., Tennis Court Road, Cambridge CB2 1QR UK
SO Current Biology, (1997) Vol. 7, No. 8, pp. 588-598.
ISSN: 0960-9822.
DT Article
LA English
AB Background: Mammalian cells deficient in the **XRCC4 DNA** repair protein are impaired in **DNA** double-strand break repair and are consequently hypersensitive to ionising radiation. These cells are also defective in site specific V(D)J recombination, a process that generates the diversity of antigen receptor genes in the developing immune system. These features are shared by cells lacking components of the **DNA**-dependent protein kinase (**DNA**-PK). immunoprecipitation and adenylylation assays demonstrated that this associated factor was the recently identified human **DNA ligase IV**. Consistent with this, **XRCC4** and **DNA ligase IV** copurified exclusively and virtually quantitatively over a variety of chromatographic steps. Protein mapping studies revealed that **XRCC4** interacted with **ligase IV** via the unique carboxy-terminal **ligase IV** extension that comprises two tandem BRCT (BRCA1 carboxyl terminus) homology motifs, which are also found in other **DNA** repair-associated factors and in the breast cancer susceptibility protein BRCA1. Conclusions: Our findings provide a function for the

carboxy-terminal region of **ligase IV** and suggest that BRCT domains of other proteins may mediate contacts between **DNA** repair components. In addition, our data implicate mammalian **ligase IV** in V(D)J recombination and the repair of radiation-induced **DNA** damage, and provide a model for the potentiation of these processes by **XRCC4**.

CC Genetics and Cytogenetics - Animal *03506
Biochemical Studies - General *10060
BC Mammalia - Unspecified *85700
IT Major Concepts
Biochemistry and Molecular Biophysics; Genetics
IT Chemicals & Biochemicals
DNA LIGASE
IT Miscellaneous Descriptors
BRCA1; BRCT DOMAIN; **DNA** DOUBLE-STRAND BREAK REPAIR PROTEIN; **DNA** END-JOINING; **DNA LIGASE IV**;
GENETICS; **XRCC4**
ORGN Super Taxa
Mammalia - Unspecified: Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mammal (Mammalia - Unspecified); Mammalia (Mammalia - Unspecified)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; vertebrates
RN **9015-85-4Q** (**DNA LIGASE**)
37259-52-2Q (**DNA LIGASE**)

L109 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:414471 BIOSIS
DN PREV199799706514
TI A newly identified **DNA ligase** of Saccharomyces cerevisiae involved in RAD52-independent repair of **DNA** double-strand breaks.
AU Schaer, Primo; Herrmann, Gernot; Daly, Graham; Lindahl, Tomas (1)
CS (1) Imperial Cancer Res. Fund, Clare Hall Lab., South Mimms UK
SO Genes & Development, (1997) Vol. 11, No. 15, pp. 1912-1924.
ISSN: 0890-9369.
DT Article
LA English
AB Eukaryotic **DNA ligases** are **ATP**-dependent **DNA** strand-joining enzymes that participate in **DNA** replication, repair, and recombination. Whereas mammalian cells contain several different **DNA ligases**, encoded by at least three distinct genes, only one **DNA ligase** has been detected previously in either budding yeast or fission yeast. Here, we describe a newly identified nonessential Saccharomyces cerevisiae gene that encodes a **DNA ligase** distinct from the CDC9 gene product. This **DNA ligase** shares significant amino acid sequence homology with human **DNA ligase IV**; accordingly, we designate the yeast gene LIG4. Recombinant LIG4 protein forms a covalent enzyme-AMP complex and can join a **DNA** single-strand break in a **DNA**/RNA hybrid duplex, the preferred substrate in vitro. Disruption of the LIG4 gene causes only marginally increased cellular sensitivity to several **DNA** damaging agents, and does not further sensitize cdc9 or rad52 mutant cells. In contrast, lig4 mutant cells have a 1000-fold reduced capacity for correct recircularization of linearized plasmids by illegitimate end-joining after transformation. Moreover, homozygous lig4 mutant diploids sporulate less efficiently than isogenic wild-type cells, and show retarded progression through meiotic prophase I. Spore viability is normal, but lig4 mutants appear to produce a higher proportion of tetrads with only three viable spores. The mutant phenotypes are consistent with functions of LIG4 in an illegitimate **DNA** end-joining pathway and ensuring efficient meiosis.
CC Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062

Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Chemical and Physical *10806
BC Ascomycetes *15100
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Genetics
IT Chemicals & Biochemicals
DNA LIGASE
IT Sequence Data
nucleotide sequence
IT Miscellaneous Descriptors
DNA; DNA LIGASE; DOUBLE STRAND BREAKS; ENZYMOLOGY; MOLECULAR GENETICS; M36067; REPAIR; X03246; X83441; X84740; X95001
ORGN Super Taxa
Ascomycetes: Fungi, Plantae
ORGN Organism Name
Saccharomyces cerevisiae (Ascomycetes)
ORGN Organism Superterms
fungi; microorganisms; nonvascular plants; plants
RN **9015-85-4Q (DNA LIGASE)**
37259-52-2Q (**DNA LIGASE**)

L109 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:413455 BIOSIS
DN PREV199799705498
TI Identification of Saccharomyces cerevisiae **DNA ligase IV**: Involvement in **DNA** double-strand break repair.
AU Teo, Soo-Hwang; **Jackson, Stephen P.**
CS Wellcome/CRC Inst., Dep. Zool., Univ. Cambridge, Tennis Court Rd., Cambridge CB2 1QR UK
SO EMBO (European Molecular Biology Organization) Journal, (1997) Vol. 16, No. 15, pp. 4788-4795.
ISSN: 0261-4189.
DT Article
LA English
AB **DNA ligases** catalyse the joining of single and double-strand **DNA** breaks, which is an essential final step in **DNA** replication, recombination and repair. Mammalian cells have four **DNA ligases**, termed **ligases** I-**IV**. In contrast, other than a **DNA ligase** I homologue (encoded by CDC9), no other **DNA ligases** have hitherto been identified in Saccharomyces cerevisiae. Here, we report the identification and characterization of a novel gene, LIG4, which encodes a protein with strong homology to mammalian **DNA ligase IV**. Unlike CDC9, LIG4 is not essential for **DNA** replication, RAD52-dependent homologous recombination nor the repair of UV light-induced **DNA** damage. Instead, it encodes a crucial component of the non-homologous end-joining (NHEJ) apparatus, which repairs **DNA** double-strand breaks that are generated by ionizing radiation or restriction enzyme digestion: a function which cannot be complemented by CDC9. Lig4p acts in the same **DNA** repair pathway as the **DNA** end-binding protein Ku. However, unlike Ku, it does not function in telomere length homeostasis. These findings indicate diversification of function between different eukaryotic **DNA ligases**. Furthermore, they provide insights into mechanisms of **DNA** repair and suggest that the NHEJ pathway is highly conserved throughout the eukaryotic kingdom.
CC Genetics and Cytogenetics - Plant *03504
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Chemical and Physical *10806
BC Ascomycetes *15100
IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Genetics

IT Chemicals & Biochemicals
DNA LIGASE
IT Sequence Data
amino acid sequence
IT Miscellaneous Descriptors
CDC9 GENE; **DNA**; **DNA** DOUBLE-STRAND BREAK REPAIR;
DNA LIGASE IV; ENZYMOLOGY; IDENTIFICATION;
KU; LIG4 GENE; L43496; MOLECULAR GENETICS; M36067; P00969;
RADIOSENSITIVITY; RECOMBINATION; REPAIR; REPLICATION; SEQUENCE
COMPARISON; U00761; U04674; X03246; X05107; X16512; X83441; X84740;
X95001; X97924; Z29716; Z73970; Z74913
ORGN Super Taxa
Ascomycetes: Fungi, Plantae
ORGN Organism Name
Saccharomyces cerevisiae (Ascomycetes)
ORGN Organism Superterms
fungi; microorganisms; nonvascular plants; plants
RN **9015-85-4Q (DNA LIGASE)**
37259-52-2Q (**DNA LIGASE**)

L109 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:392522 BIOSIS
DN PREV199799691725
TI Activity of **DNA ligase IV** stimulated by
complex formation with **XRCC4** protein in mammalian cells.
AU Grawunder, Ulf; Wilm, Matthias; Wu, Xiantuo; Kulesza, Peter; Wilson,
Thomas E.; Mann, Matthias; Lieber, Michael R. (1)
CS (1) Norris Comprehensive Cancer Cent., Univ. Southern Calif., Room 5425,
Mailstop 73, 1441 Eastlake Ave., Los Angeles, CA 90033 USA
SO Nature (London), (1997) Vol. 388, No. 6641, pp. 492-495.
ISSN: 0028-0836.
DT Article
LA English
AB Mutation of the **XRCC4** gene in mammalian cells prevents the
formation of the signal and coding joints in the V(D)J recombination
reaction, which is necessary for production of a functional immunoglobulin
gene, and renders the cells highly sensitive to ionizing radiation.
However, **XRCC4** shares no sequence homology with other proteins,
nor does it have a biochemical activity to indicate what its function
might be. Here we show that **DNA ligase IV**
(ref. 5) co-immunoprecipitates with **XRCC4** and that these two
proteins specifically interact with one another in a yeast two-hybrid
system. Ligation of **DNA** double-strand breaks in a cell-free
system by **DNA ligase IV** is increased
fivefold by purified **XRCC4** and seven- to eightfold when
XRCC4 is co-expressed with **DNA ligase**
IV. We conclude that the biological consequences of mutating
XRCC4 are primarily due to the loss of its stimulatory effect on
DNA ligase IV. the function of the
XRCC4-DNA ligase IV complex may be
to carry out the final steps of V(D)J recombination and joining of
DNA ends.
CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
*34508
BC Cricetidae *86310
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Genetics; Immune
System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
DNA LIGASE; LIGASE
IT Miscellaneous Descriptors

DBA LIGASE; IMMUNE SYSTEM; MOLECULAR GENETICS; V(D)J RECOMBINATION REACTION; XR-1 CELL LINE; **XRCC4** PROTEIN

ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
CHINESE HAMSTER OVARY (Cricetidae): cell line

ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

RN **9015-85-4Q (DNA LIGASE)**
37259-52-2Q (**DNA LIGASE**)
9031-56-5Q (**LIGASE**)
9080-13-1Q (**LIGASE**)

L109 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:507086 BIOSIS
DN PREV199699229442
TI **DNA ligase IV** from HeLa cell nuclei.
AU Robins, Peter; Lindahl, Tomas (1)
CS (1) Imperial Cancer Res. Fund, Clare Hall Lab., South Mimms, Hertfordshire EN6 3LD UK
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 39, pp. 24257-24261. ISSN: 0021-9258.
DT Article
LA English
AB A human cDNA encoding a previously unrecognized **DNA ligase IV** has been identified (Wei, Y.-F., Robins, P., Carter, K, Caldecott, K, Pappin, D. J. C., Yu, G.-L, Wang, R.-P., Shell, B. K., Nash, R. A., Schar, P., Barnes, D. E., Haseltine, W. A., and Lindahl, T. (1995) Mol. Cell. Biol. 15, 3206-3216). Antibodies have been raised against predicted peptide sequences of **DNA ligase IV** and used to identify the enzyme during purification from HeLa cell nuclei. The 96-kDa **DNA ligase IV** and the 103-kDa **DNA ligase** III co-migrate during SDS-polyacrylamide gel electrophoresis and have similar column fractionation properties, which complicates the distinction between the two enzymes, but they have been separated by Mono S liquid chromatography. During initial size fractionation by gel chromatography in 1 M NaCl, **DNA ligase IV** elutes in the same position as the **DNA ligase** III-XRCC1 protein complex, indicating that **DNA ligase IV** is also bound to another protein or occurs as a dimer. **DNA ligase IV** has been purified free from other **DNA ligases**, and its enzymatic properties have been examined. The purified protein effectively joins single-strand breaks in a double-stranded polydeoxynucleotide in an **ATP**-dependent reaction. The substrate specificity of **DNA ligase IV** differs from those of the other two cloned human **DNA ligases**, I and III, with regard to their ability to join the hybrid substrates oligo(dT) cntdot poly(rA) and oligo(rA) cntdot poly(dT). **DNA ligase IV** occurs in part as an enzyme-adenylate complex in HeLa cell nuclear extracts.
CC Cytology and Cytochemistry - Human *02508
Comparative Biochemistry, General *10010
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - General and Comparative Studies; Coenzymes *10802
Enzymes - Chemical and Physical *10806
In Vitro Studies, Cellular and Subcellular *32600
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics)
IT Chemicals & Biochemicals
DNA LIGASE

IT Miscellaneous Descriptors
COMPLEMENTARY **DNA**; **DNA LIGASE** I; **DNA LIGASE** III; **DNA LIGASE IV**; ENZYMOLOGY
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
HELA (Hominidae): cell line
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN **9015-85-4Q (DNA LIGASE)**
37259-52-2Q (**DNA LIGASE**)

L109 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:298466 BIOSIS
DN PREV199598312766
TI Molecular cloning and expression of human cDNAs encoding a novel **DNA ligase IV** and **DNA ligase** III, an enzyme active in **DNA** repair and recombination.
AU Wei, Ying-Fei; Robins, Peter; Carter, Kenneth; Caldecott, Keith; Pappin, Darryl J. C.; Yu, Guo-Liang; Wang, Rui-Ping; Shell, Brenda K.; Nash, Rachel A.; Schar, Primo; Barnes, Deborah E.; Haseltine, William A.; Lindahl, Tomas (1)
CS (1) Imperial Cancer Res. Fund, Clare Hall Lab., South Mimms, Hertfordshire EN6 3LD UK
SO Molecular and Cellular Biology, (1995) Vol. 15, No. 6, pp. 3206-3216. ISSN: 0270-7306.
DT Article
LA English
AB Three distinct **DNA ligases**, I to III, have been found previously in mammalian cells, but a cloned cDNA has been identified only for **DNA ligase** I, an essential enzyme active in **DNA** replication. A short peptide sequence conserved close to the C terminus of all known eukaryotic **DNA ligases** was used to search for additional homologous sequences in human cDNA libraries. Two different incomplete cDNA clones that showed partial homology to the conserved peptide were identified. Full-length cDNAs were obtained and expressed by in vitro transcription and translation. The 103-kDa product of one cDNA clone formed a characteristic complex with the XRCC1 **DNA** repair protein and was identical with the previously described **DNA ligase** III. **DNA ligase** III appears closely related to the smaller **DNA ligase** II. The 96-kDa in vitro translation product of the second cDNA clone was also shown to be an **ATP-dependent DNA ligase**. A fourth **DNA ligase** (**DNA ligase IV**) has been purified from human cells and shown to be identical to the 96-kDa **DNA ligase** by unique agreement between mass spectrometry data on tryptic peptides from the purified enzyme and the predicted open reading frame of the cloned cDNA. The amino acid sequences of **DNA ligases** III and **IV** share a related active-site motif and several short regions of homology with **DNA ligase** I, other **DNA ligases**, and RNA capping enzymes. **DNA ligases** III and **IV** are encoded by distinct genes located on human chromosomes 17q11.2-12 and 13q33-34, respectively.
CC Genetics and Cytogenetics - Human *03508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Chemical and Physical *10806
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and

Molecular Biophysics); Genetics; Metabolism
IT Chemicals & Biochemicals
DNA LIGASE
IT Sequence Data
amino acid sequence; molecular sequence data
IT Miscellaneous Descriptors
COMPLEMENTARY DNA; OPEN READING FRAME; SEQUENCE HOMOLOGY; XRCC1 DNA REPAIR PROTEIN
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN **9015-85-4Q (DNA LIGASE)**
37259-52-2Q (**DNA LIGASE**)

=> fil embase

FILE 'EMBASE' ENTERED AT 13:37:08 ON 04 JAN 2001
COPYRIGHT (C) 2001 Elsevier Science B.V. All rights reserved.

FILE COVERS 1974 TO 29 Dec 2000 (20001229/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L151 ANSWER 1 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 97238862 EMBASE
DN 1997238862
TI A newly identified **DNA ligase** of Saccharomyces cerevisiae involved in RAD52-independent repair of **DNA** double-strand breaks.
AU Schar P.; Herrmann G.; Daly G.; Lindahl T.
CS T. Lindahl, Imperial Cancer Research Fund, Clare Hall Laboratories, South Mimms, United Kingdom. lindahl@icrf.icnet.uk
SO Genes and Development, (1997) 11/15 (1912-1924).
Refs: 55
ISSN: 0890-9369 CODEN: GEDEEP
CY United States
DT Journal; Article
FS 016 Cancer
022 Human Genetics
LA English
SL English
AB Eukaryotic **DNA ligases** are ATP-dependent **DNA** strand-joining enzymes that participate in **DNA** replication, repair, and recombination. Whereas mammalian cells contain several different **DNA ligases**, encoded by at least three distinct genes, only one **DNA ligase** has been detected previously in either budding yeast or fission yeast. Here, we describe a newly identified nonessential Saccharomyces cerevisiae gene that encodes a **DNA ligase** distinct from the CDC9 gene product. This **DNA ligase** shares significant amino acid sequence homology with human **DNA ligase IV**; accordingly, we designate the yeast gene LIG4. Recombinant LIG4 protein forms a covalent enzyme-AMP complex and can join a **DNA** single-strand break in a **DNA**/RNA hybrid duplex, the preferred substrate in vitro. Disruption of the LIG4 gene causes only marginally increased cellular sensitivity to several **DNA** damaging agents,

and does not further sensitize cdc9 or rad52 mutant cells. In contrast, lig4 mutant cells have a 1000-fold reduced capacity for correct recircularization of linearized plasmids by illegitimate end-joining after transformation. Moreover, homozygous lig4 mutant diploids sporulate less efficiently than isogenic wild-type cells, and show retarded progression through meiotic prophase I. Spore viability is normal, but lig4 mutants appear to produce a higher proportion of tetrads with only three viable spores. The mutant phenotypes are consistent with functions of LIG4 in an illegitimate **DNA** end- joining pathway and ensuring efficient meiosis.

CT Medical Descriptors:
*dna repair
*dna strand breakage
article
dna replication
enzyme activity
meiosis
nonhuman
priority journal
saccharomyces cerevisiae
Drug Descriptors:
*double stranded dna
***polydeoxyribonucleotide synthase**
RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 2 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 97235439 EMBASE
DN 1997235439
TI Yeast **DNA ligase IV** mediates non-homologous **DNA** end joining.
AU Wilson T.E.; Grawunder U.; Lieber M.R.
CS M.R. Lieber, Washington Univ. Sch. of Med., Division of Laboratory Medicine, Department of Pathology, 660 S. Euclid Avenue, St Louis, MO 63210, United States
SO Nature, (1997) 388/6641 (495-498).
Refs: 24
ISSN: 0028-0836 CODEN: NATUAS
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
029 Clinical Biochemistry
LA English
SL English
AB The discovery of homologues from the yeast Saccharomyces cerevisiae of the human Ku **DNA**-end-binding proteins (*HDF1* and *KU80*) has established that this organism is capable of non-homologous double-strand end joining (NHEJ), a form of **DNA** double-strand break repair (DSBR) active in mammalian V(D)J recombination. Identification of the **DNA ligase** that mediates NHEJ in yeast will help elucidate the function of the four mammalian **DNA ligases** in DSBR, V(D)J recombination and other reactions. Here we show that S. cerevisiae has two typical **DNA ligases**, the known **DNA ligase** I homologue CDC9 (refs 11-14) and the previously unknown **DNA ligase IV** homologue DNL4. dnl4 mutants are deficient in precise and end-processed NHEJ. DNL4 and HDF1 are epistatic in this regard, with the mutation of each having equivalent effects. dnl4 mutants are complemented by overexpression of Dnl4 but not of Cdc9, and deficiency of Dnl4 alone does not impair either cell growth or the Cdc9- mediated responses to ionizing and ultraviolet radiation. Thus, S. cerevisiae has two distinct and separate ligation pathways.
CT Medical Descriptors:
*dna repair
article
dna strand breakage
enzyme activity

ionizing radiation
mutation
nonhuman
priority journal
saccharomyces cerevisiae
ultraviolet radiation
Drug Descriptors:
*dna
***polydeoxyribonucleotide synthase**
RN (dna) 9007-49-2; (**polydeoxyribonucleotide synthase**)
9015-85-4

L151 ANSWER 3 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 97235438 EMBASE
DN 1997235438
TI Activity of **DNA ligase IV** stimulated by complex formation with XRCC4 protein in mammalian cells.
AU Grawunder U.; Wilm M.; Wu X.; Kulesza P.; Wilson T.E.; Mann M.; Lieber M.R.
CS M.R. Lieber, Washington Univ. Sch. of Medicine, Division of Molecular Oncology, Department of Pathology, 660 South Euclid Avenue, St Louis, MO 63110, United States
SO Nature, (1997) 388/6641 (492-495).
Refs: 30
ISSN: 0028-0836 CODEN: NATUAS
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Mutation of the XRCC4 gene in mammalian cells prevents the formation of the signal and coding joints in the V(D)J recombination reaction, which is necessary for production of a functional immunoglobulin gene, and renders the cells highly sensitive to ionizing radiation. However, XRCC4 shares no sequence homology with other proteins, nor does it have a biochemical activity to indicate what its function might be. Here we show that **DNA ligase IV** (ref. 5) co-immunoprecipitates with XRCC4 and that these two proteins specifically interact with one another in a yeast two-hybrid system. Ligation of **DNA** double-strand breaks in a cell- free system by **DNA ligase IV** is increased five fold by purified XRCC4 and seven- to eight fold when XRCC4 is co-expressed with **DNA ligase IV**. We conclude that the biological consequences of mutating XRCC4 are primarily due to the loss of its stimulatory effect on **DNA ligase IV**: the function of the XRCC4-**DNA ligase IV** complex may be to carry out the final steps of V(D)J recombination and joining of **DNA** ends.
CT Medical Descriptors:
*enzyme binding
*protein protein interaction
article
cell free system
dna strand breakage
enzyme activity
gene mutation
genetic recombination
mammal cell
nonhuman
priority journal
protein binding
radiosensitivity
Drug Descriptors:
***polydeoxyribonucleotide synthase**
RN (**polydeoxyribonucleotide synthase**) **9015-85-4**

L151 ANSWER 4 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 97233149 EMBASE
DN 1997233149
TI Identification of saccharomyces cerevisiae **DNA ligase IV**: Involvement in **DNA** double-strand break repair.
AU Teo S.-H.; Jackson S.P.
CS S.-H. Teo, Wellcome-CRC Institute, University of Cambridge, Tennis Court Road, Cambridge CB2 1QR, United Kingdom. sht@mole.bio.cam.ac.uk
SO EMBO Journal, (1997) 16/15 (4788-4795).
Refs: 49
ISSN: 0261-4189 CODEN: EMJODG
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
029 Clinical Biochemistry
LA English
SL English
AB **DNA ligases** catalyse the joining of single and doublestrand **DNA** breaks, which is an essential final step in **DNA** replication, recombination and repair. Mammalian cells have four **DNA ligases**, termed **ligases** I-**IV**. In contrast, other than a **DNA ligase** I homologue (encoded by CDC9), no other **DNA ligases** have hitherto been identified in Saccharomyces cerevisiae. Here, we report the identification and characterization of a novel gene, LIG4, which encodes a protein with strong homology to mammalian **DNA ligase IV**. Unlike CDC9, LIG4 is not essential for **DNA** replication, RAD52-dependent homologous recombination nor the repair of UV light-induced **DNA** damage. Instead, it encodes a crucial component of the non-homologous end-joining (NHEJ) apparatus, which repairs **DNA** double-strand breaks that are generated by ionizing radiation or restriction enzyme digestion: a function which cannot be complemented by CDC9. Lig4p acts in the same **DNA** repair pathway as the **DNA** end-binding protein Ku. However, unlike Ku, it does not function in telomere length homeostasis. These findings indicate diversification of function between different eukaryotic **DNA ligases**. Furthermore, they provide insights into mechanisms of **DNA** repair and suggest that the NHEJ pathway is highly conserved throughout the eukaryotic kingdom.
CT Medical Descriptors:
*dna repair
*dna strand breakage
*saccharomyces cerevisiae
article
controlled study
dna damage
dna recombination
dna replication
ionizing radiation
nonhuman
priority journal
sequence homology
Drug Descriptors:
*double stranded dna: EC, endogenous compound
***polydeoxyribonucleotide synthase: EC, endogenous compound**
dna binding protein: EC, endogenous compound
restriction endonuclease
single stranded dna: EC, endogenous compound
RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 5 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 97215475 EMBASE
DN 1997215475
TI Two distinct **DNA ligase** activities in mitotic extracts of the yeast Saccharomyces cerevisiae.
AU Ramos W.; Tappe N.; Talamantez J.; Friedberg E.C.; Tomkinson A.E.
CS A.E. Tomkinson, Institute of Biotechnology, Institute of Biotechnology,

Univ Texas Hlth Sci Ctr San Antonio, 15355 Lambda Drive, San Antonio, TX 78245, United States. tomkinson@uthscsa.edu
SO Nucleic Acids Research, (1997) 25/8 (1485-1492).
Refs: 44
ISSN: 0305-1048 CODEN: NARHAD
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
029 Clinical Biochemistry
LA English
SL English
AB Four biochemically distinct **DNA ligases** have been identified in mammalian cells. One of these enzymes, **DNA ligase** I, is functionally homologous to the **DNA ligase** encoded by the Saccharomyces cerevisiae CDC9 gene. Cdc9 **DNA ligase** has been assumed to be the only species of **DNA ligase** in this organism. In the present study we have identified a second **DNA ligase** activity in mitotic extracts of S. cerevisiae with chromategraphic properties different from Cdc9 **DNA ligase**, which is the major **DNA** joining activity. This minor **DNA** joining activity, which contributes 5-10% of the total cellular **DNA** joining activity, forms a 90 kDa enzyme-adenylate intermediate which, unlike the Cdc9 enzyme-adenylate intermediate, reacts with an oligo (pdT)/poly (rA) substrate. The levels of the minor **DNA** joining activity are not altered by mutation or by overexpression of the CDC9 gene. Furthermore, the 90 kDa polypeptide is not recognized by a Cdc9 antiserum. Since this minor species does not appear to be a modified form of Cdc9 **DNA ligase**, it has been designated as S. cerevisiae **DNA ligase** II. Based on the similarities in polynucleotide substrate specificity, this enzyme may be the functional homolog of mammalian **DNA ligase** III or **IV**.
CT Medical Descriptors:
*saccharomyces cerevisiae
article
chromatography
controlled study
enzyme activity
gene expression
gene mutation
mitosis
nonhuman
priority journal
sequence homology
Drug Descriptors:
***polydeoxyribonucleotide synthase: EC, endogenous compound**
polypeptide
RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 6 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 96300354 EMBASE
DN 1996300354
TI **DNA ligase IV** from HeLa cell nuclei.
AU Robins P.; Lindahl T.
CS Clare Hall Laboratories, Imperial Cancer Research Fund, South Mimms,Hertfordshire EN6 3LD, United Kingdom
SO Journal of Biological Chemistry, (1996) 271/39 (24257-24261).
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB A human cDNA encoding a previously unrecognized **DNA ligase IV** has been identified (Wei, Y.-F., Robins, P., Carter, K., Caldecott, K., Pappin, D. J. C., Yu, G.-L., Wang, R.-P.,

Shell, B. K., Nash, R. A., Schar, P., Barnes, D. E., Haseltine, W. A., and Lindahl, T. (1995) Mol. Cell. Biol. 15, 3206 - 3216). Antibodies have been raised against predicted peptide sequences of **DNA ligase IV** and used to identify the enzyme during purification from HeLa cell nuclei. The 96-kDa **DNA ligase IV** and the 103-kDa **DNA ligase** III co-migrate during SDS-polyacrylamide gel electrophoresis and have similar column fractionation properties, which complicates the distinction between the two enzymes, but they have been separated by Mono S liquid chromatography. During initial size fractionation by gel chromatography in 1 M NaCl, **DNA ligase IV** elutes in the same position as the **DNA ligase** III-XRCC1 protein complex, indicating that **DNA ligase IV** is also bound to another protein or occurs as a dimer. **DNA ligase IV** has been purified free from other **DNA ligases**, and its enzymatic properties have been examined. The purified protein effectively joins single-strand breaks in a double-stranded polydeoxynucleotide in an ATP-dependent reaction. The substrate specificity of **DNA ligase IV** differs from those of the other two cloned human **DNA ligases**, I and III, with regard to their ability to join the hybrid substrates oligo(dT).cntdot.poly(rA) and oligo(rA).cntdot.poly(dT). **DNA ligase IV** occurs in part as an enzyme-adenylate complex in HeLa cell nuclear extracts.

CT Medical Descriptors:
*cell nucleus
*enzyme analysis
*hela cell
amino acid sequence
article
carboxy terminal sequence
dna sequence
dna strand breakage
enzyme purification
enzyme specificity
human
human cell
liquid chromatography
polyacrylamide gel electrophoresis
priority journal
protein analysis
sequence analysis
Drug Descriptors:
***polydeoxyribonucleotide synthase**
RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 7 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 96237420 EMBASE
DN 1996237420
TI **DNA ligase** I is required for fetal liver erythropoiesis but is not essential for mammalian cell viability.
AU Bentley D.J.; Selfridge J.; Millar J.K.; Samuel K.; Hole N.; Ansell J.D.; Melton D.W.
CS Institute of Cell/Molecular Biology, Darwin Building, University of Edinburgh, Mayfield Road,Edinburgh EH9 3JR, United Kingdom
SO Nature Genetics, (1996) 13/4 (489-491).
ISSN: 1061-4036 CODEN: NGENEC
CY United States
DT Journal; Article
FS 022 Human Genetics
LA English
SL English
AB Four distinct **DNA ligase** activities (I-**IV**) have been identified within mammalian cells. Evidence has indicated that **DNA ligase** I is central to **DNA** replication, as well as being involved in **DNA** repair processes. A patient with

altered **DNA ligase** I displayed a phenotype similar to Bloom's syndrome, being immunodeficient, growth retarded and predisposed to cancer. Fibroblasts isolated from this patient (46BR) exhibited abnormal lagging strand synthesis and repair deficiency. It has been reported that **DNA ligase** I is essential for cell viability, but here we show that cells lacking **DNA ligase** I are in fact viable. Using gene targeting in embryonic stem (ES) cells, we have produced **DNA ligase** I-deficient mice. Embryos develop normally to mid-term, when haematopoiesis usually switches to the fetal liver. Thereupon acute anaemia develops, despite the presence of erythroid-committed progenitor cells in the liver. Thus **DNA ligase** I is required for normal development, but is not essential for replication. Hence a previously unsuspected redundancy must exist between mammalian **DNA ligases.**

CT Medical Descriptors:
*cell viability
*erythropoiesis
anemia
animal cell
animal tissue
article
bloom syndrome
dna replication
embryo
enzyme activity
fetus liver
gene targeting
hematopoiesis
mouse
nonhuman
priority journal
Drug Descriptors:
***polydeoxyribonucleotide synthase**
RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 8 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 95156035 EMBASE
DN 1995156035
TI Molecular cloning and expression of human cDNAs encoding a novel **DNA ligase IV** and **DNA ligase** III, an enzyme active in **DNA** repair and recombination.
AU Wei Y.-F.; Robins P.; Carter K.; Caldecott K.; Pappin D.J.C.; Yu G.-L.; Wang - R.P.; Shell B.K.; Nash R.A.; Schar P.; Barnes D.E.; Haseltine W.A.; Lindahl T.
CS Imperial Cancer Research Fund, Clare Hall Laboratories,South Mimms, Hertfordshire EN6 3LD, United Kingdom
SO Molecular and Cellular Biology, (1995) 15/6 (3206-3216).
ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Three distinct **DNA ligases**, I to III, have been found previously in mammalian cells, but a cloned cDNA has been identified only for **DNA ligase** I, an essential enzyme active in **DNA** replication. A short peptide sequence conserved close to the C terminus of all known eukaryotic **DNA ligases** was used to search for additional homologous sequences in human cDNA libraries. Two different incomplete cDNA clones that showed partial homology to the conserved peptide were identified. Full-length cDNAs were obtained and expressed by in vitro transcription and translation. The 103-kDa product of one cDNA clone formed a characteristic complex with the XRCC1 **DNA** repair protein and was identical with the previously described **DNA ligase** III. **DNA ligase** III

appears closely related to the smaller **DNA ligase** II.
The 96-kDa in vitro translation product of the second cDNA clone was also shown to be an **ATP-dependent DNA ligase**. A fourth **DNA ligase** (**DNA ligase IV**) has been purified from human cells and shown to be identical to the 96-kDa **DNA ligase** by unique agreement between mass spectrometry data on tryptic peptides from the purified enzyme and the predicted open reading frame of the cloned cDNA. The amino acid sequences of **DNA ligases** III and **IV** share a related active- site motif and several short regions of homology with **DNA ligase** I, other **DNA ligases**, and RNA capping enzymes. **DNA ligases** III and **IV** are encoded by distinct genes located on human chromosomes 17q11.2-12 and 13q33-34, respectively.

CT Medical Descriptors:
*dna recombination
*dna repair
*enzyme analysis
amino acid sequence
animal cell
animal tissue
article
cattle
chromosome 13q
chromosome 17q
controlled study
enzyme active site
fluorescence in situ hybridization
genetic transcription
hela cell
human
human cell
human tissue
mammal cell
mass spectrometry
nonhuman
open reading frame
priority journal
rna capping
rna translation
sequence homology
tissue distribution
Drug Descriptors:
*adenosine triphosphate
*complementary dna: EC, endogenous compound
***polydeoxyribonucleotide synthase*: EC, endogenous compound**
*rna polymerase: EC, endogenous compound
messenger rna: EC, endogenous compound
polydeoxyribonucleotide synthase iii: EC, endogenous compound
polydeoxyribonucleotide synthase iv: EC, endogenous compound
unclassified drug

RN (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (**polydeoxyribonucleotide synthase**) **9015-85-4**; (rna polymerase) 9014-24-8

L151 ANSWER 9 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 94016102 EMBASE
DN 1994016102
TI Cloning of the large subunit of activator 1 (replication factor C) reveals homology with bacterial **DNA ligases**.
AU Burbelo P.D.; Utani A.; Pan Z.-Q.; Yamada Y.
CS Laboratory of Developmental Biology, Natl. Institute of Dental Research, National Institutes of Health,Bethesda, MD 20892, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (1993) 90/24 (11543-11547).
ISSN: 0027-8424 CODEN: PNASA6

CY United States
DT Journal; Article
FS 022 Human Genetics
LA English
SL English
AB We have cloned a gene encoding a **DNA**-binding protein by Southwestern screening of a murine cDNA library with a double-stranded oligonucleotide containing the sequence from the bidirectional promoter of the .alpha.1 and .alpha.2 collagen **IV** genes. The middle portion of this 1131-amino acid protein has a region homologous to bacterial **DNA ligases**, and the more carboxyl portion contains several domains homologous to p40, p38, p37, and p36.5 subunits of activator 1 (A1, also called replication factor C), a human replication protein complex. Western blotting revealed that antiserum generated against part of the recombinant protein reacted specifically with the 145-kDa component of the purified human A1 complex, indicating that it is the murine counterpart of the A1 p145. Characterization of the **DNA** -binding activity of the recombinant fusion protein by gel mobility-shift assay revealed that it had a preference for a run of pyrimidines on one strand. Deletion analysis using recombinant proteins revealed that the **DNA ligase**-like domain was required for **DNA** -binding activity. The finding that the region required for the binding of murine A1 p145 to **DNA** has similarity to a domain found in **DNA ligases** suggests that this region may be utilized by both proteins in recognizing **DNA**.
CT Medical Descriptors:
*molecular cloning
*sequence homology
animal cell
article
binding affinity
dna binding
dna replication
molecular recognition
mouse
nonhuman
priority journal
promoter region
protein domain
protein quaternary structure
Drug Descriptors:
binding protein
*bacterial dna
***polydeoxyribonucleotide synthase**
RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 10 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 93352622 EMBASE
DN 1993352622
TI Cloning and gene map assignment of the Xiphophorus **DNA ligase** 1 gene.
AU Walter R.B.; Rolig R.L.; Kozak K.A.; McEntire B.; Morizot D.C.; Nairn R.S.
CS Department of Biology, Southwest Texas State University, Aquarena Springs Drive,San Marcos, TX 78666, United States
SO Molecular Biology and Evolution, (1993) 10/6 (1227-1238).
ISSN: 0737-4038 CODEN: MBEVEO
CY United States
DT Journal; Article
FS 021 Developmental Biology and Teratology
022 Human Genetics
LA English
SL English
AB Fishes represent the stem vertebrate condition and have maintained several gene arrangements common to mammalian genomes throughout the 450 Myr of divergence from a common ancestor. One such syntenic arrangement includes the GPI-PEPD enzyme association on Xiphophorus linkage group **IV**

and human chromosome 19. Previously we assigned the Xiphophorus homologue of the human ERCC2 gene to linkage group U5 in tight association with the CKM locus. CKM is also tightly linked to the ERCC2 locus on human chromosome 19, leading to speculation that human chromosome 19 may have arisen by fusion of two ancestral linkage groups which have been maintained in fishes. To investigate this hypothesis further, we isolated and sequenced Xiphophorus fish genomic regions exhibiting considerable sequence similarity to the human **DNA ligase** 1 amino acid sequence. Comparison of the fish **DNA ligase** sequence with those of other species suggests several modes of amino acid conservation in this gene. A 2.2-kb restriction fragment containing part of an X. moculatus **DNA ligase** 1 exon was used in backcross hybrid mapping with 12 enzyme or RFLP loci. Significant linkage was observed between the nucleoside phosphorylase (NP2) and the **DNA ligase** (LIG1) loci on Xiphophorus linkage group VI. This assignment suggests that the association of four **DNA** repair-related genes on human chromosome 19 may be the result of chance chromosomal rearrangements.

CT Medical Descriptors:
*gene assignment
article
chromosome 19
fish
gene isolation
gene mapping
gene rearrangement
gene sequence
genetic linkage
molecular cloning
nonhuman
sequence homology
Drug Descriptors:
***polydeoxyribonucleotide synthase**

RN **(polydeoxyribonucleotide synthase) 9015-85-4**

L151 ANSWER 11 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 89010823 EMBASE
DN 1989010823
TI Amplification of cloned DNA as tandem multimers using BspMI-generated asymmetric cohesive ends.
AU Kim S.C.; Szybalski W.
CS McArdle Laboratory for Cancer Research, University of Wisconsin, Madison, WI 53706, United States
SO Gene, (1988) 71/1 (1-8).
ISSN: 0378-1119 CODEN: GENED6
CY Netherlands
DT Journal
FS 022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
AB By generating totally asymmetric and complementary cohesive ends it is possible to amplify any cloned **DNA** fragment, while assuring that all repeating units are ligated in the same orientation. Starting with plasmid pUC18, which contains a unique BspMI site, an amplification plasmid, pSK3, was constructed in which a multiple cloning site (MCS) is flanked by two BspMI recognition sites with identical cut sites, creating the complementary 5'-ATGC and 5'-GCAT single-stranded ends. Any **DNA** fragment cloned into the MCS could be amplified by (i) excision with BspMI, (ii) fragment isolation, (iii) self-ligation of the fragments using T4 **DNA ligase**, (iv) selection of multimers of desired length, and (v) cloning them into the BspMI-digested original plasmid. Using this procedure, plasmids carrying either 30 copies of the 60-bp MCS fragment (a control experiment) or ten copies of the 1.2-kb lux A gene fragment were constructed. The plasmids were stable since all the repeat units were in the same orientation, as

determined by restriction analysis. Potentially, not only BspMI but other class-IIS restriction enzymes (with recognition sites separated by a fixed distance from the staggered cut points) could be applied, preferably those that create 4-to-5-nucleotide-long cohesive ends and utilize rather rare recognition sites.

CT Medical Descriptors:
*gene amplification
*molecular cloning
heredity
plasmid
genetic engineering
nonhuman
methodology
priority journal
Drug Descriptors:
*recombinant dna
*restriction endonuclease

L151 ANSWER 12 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 80102162 EMBASE
DN 1980102162
TI Changes of **DNA ligases** in chick neural retina as a function of age.
AU David J.C.; Pieau C.; Carre D.S.
CS Dept. Biochim. Developpem., IBBM, Univ. Paris VII, 75221 Paris Cedex 05, France
SO Differentiation, (1979) 15/3 (169-175).
CODEN: DFFNAW
CY Germany
DT Journal
FS 021 Developmental Biology and Teratology
020 Gerontology and Geriatrics
012 Ophthalmology
029 Clinical Biochemistry
LA English
AB In the course of chick neural retina development, several forms of **DNA ligase** have been found. During embryonic life the major **DNA ligase** activity that is found at seven days is form I (8.2 S) which gradually decreases and disappears by 14 days after incubation, whereas form II (6.2 S) increases to reach a maximum at the time of hatching. Form II then decreases reaching a constant level by Day 7 and from that time new slow sedimenting forms also appear (forms III and **IV**). Form III (2 S) is first detectable at seven days and increases up to 90 days, whereas form **IV** (3 S) is the only form detected in the 17- and 18-month-old and also in the 5-year-old birds. These four forms display different elution patterns on phosphocellulose column chromatography. They also differ in their thermal stability and sensitivity towards N-ethylmaleimide.
CT Medical Descriptors:
*age
*retina neuroepithelial layer
animal experiment
chicken
visual system
Drug Descriptors:
*dna
***polydeoxyribonucleotide synthase**
RN (dna) 9007-49-2; (**polydeoxyribonucleotide synthase**) **9015-85-4**

=> fil wpids

FILE 'WPIDS' ENTERED AT 13:56:24 ON 04 JAN 2001
COPYRIGHT (C) 2001 DERWENT INFORMATION LTD

FILE LAST UPDATED: 30 DEC 2000 <20001230/UP>
>>>UPDATE WEEKS:
MOST RECENT DERWENT WEEK 200101 <200101/DW>
DERWENT WEEK FOR CHEMICAL CODING: 200101
DERWENT WEEK FOR POLYMER INDEXING: 200101
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> D COST AND SET NOTICE DO NOT REFLECT SUBSCRIBER DISCOUNTS - SEE HELP COST <<<

>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY RESOURCE, PLEASE VISIT http://www.derwent.com/chemistryresource/index.html <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://www.derwent.com/covcodes.html <<<

=> d all abeq tech

L186 ANSWER 1 OF 1 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-399301 [34] WPIDS
CR 1998-379674 [33]
DNN N1998-310586 DNC C1998-121060
TI Modulation of cellular DNA repair activity - using compounds identified as modulating the interaction of **XRCC4**, **DNA ligase IV** and DNA-**PKcs/Ku**.
DC B04 D16 S03
IN CRITCHLOW, S E; JACKSON, S P
PA (CANC-N) CANCER RES CAMPAIGN TECHNOLOGY
CYC 82
PI WO 9830902 A1 19980716 (199834)* EN 118p G01N033-50 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
GB 2322193 A 19980819 (199835) G01N033-68 <--
AU 9855681 A 19980803 (199850) G01N033-50 <--
GB 2329248 A 19990317 (199913) G01N033-68 <--
GB 2329469 A 19990324 (199914) G01N033-68 <--
GB 2329248 B 19990922 (199941) G01N033-68 <--
GB 2329469 B 19990922 (199941) G01N033-68 <--
GB 2322193 B 19990929 (199942) G01N033-68 <--
EP 966683 A1 19991229 (200005) EN G01N033-50 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 724108 B 20000914 (200051) G01N033-50 <--
ADT WO 9830902 A1 WO 1998-GB95 19980113; GB 2322193 A GB 1998-663 19980113; AU 9855681 A AU 1998-55681 19980113; GB 2329248 A Derived from GB 1998-663 19980113, GB 1998-20952 19980925; GB 2329469 A Derived from GB 1998-663 19980113, GB 1998-20948 19980925; GB 2329248 B Derived from GB 1998-663 19980113, GB 1998-20952 19980925; GB 2329469 B Derived from GB 1998-663 19980113, GB 1998-20948 19980925; GB 2322193 B GB 1998-663 19980113; EP 966683 A1 EP 1998-900589 19980113, WO 1998-GB95 19980113; AU 724108 B AU 1998-55681 19980113
FDT AU 9855681 A Based on WO 9830902; EP 966683 A1 Based on WO 9830902; AU 724108 B Previous Publ. AU 9855681, Based on WO 9830902
PRAI GB 1997-13131 19970620; GB 1997-574 19970113
IC ICM **G01N033-50**; **G01N033-68**
ICS C12N009-12; C12Q001-48
AB WO 9830902 A UPAB: 20001016
Assaying for a compound able to modulate the interaction or **binding** between **XRCC4** and any of **DNA ligase IV** and/or DNA-**PKcs/Ku** (DPK) comprises: (a) bringing into contact: (i) a substance including

XRCC4 (or a fragment, derivative, variant or analogue able to **bind DNA ligase IV** or DPK); (ii) a substance including **DNA ligase IV** (or a fragment, derivative, variant or analogue able to **bind XRCC4**; and/or (iii) DPK (or a fragment, derivative, variant or analogue able to **bind XRCC4**), and a test compound under conditions where, if the test compound is not an inhibitor of interaction or **binding** between the substances, the substances interact or **bind**; and (b) determining interaction or **binding** between the substances.

Also claimed are: (1) assaying for a compound able to affect **DNA ligase IV** activity, comprising: (a) bringing into contact **DNA ligase IV** and a test compound; and (b) determining **DNA ligase** activity; (2) an assay method including: (a) bringing into contact: (i) a substance which includes DPK or a fragment, derivative, variant or analogue able to **phosphorylate XRCC4**; (ii) a substance which includes **XRCC4** or a fragment, derivative, variant or analogue able to **bind XRCC4** including a site **phosphorylated** by DPK; and (iii) a test compound; and (b) determining **phosphorylation** at the site; (3) an agent capable of: (a) modulating the interaction between **XRCC4** and any of **DNA ligase IV** and/or DPK; (b) affecting **DNA ligase IV** activity; or (c) affecting DPK **phosphorylation** of **XRCC4**, obtained using a method as above; (4) a peptide fragment (A) of **DNA ligase IV** capable of modulating interaction between **XRCC4** and any of **DNA ligase IV** and/or DPK; (5) a nucleic acid (I) encoding (A); (6) a peptide fragment of **XRCC4** (B) capable of modulating interaction between **XRCC4** and **DNA ligase IV**; (7) a nucleic acid (II) encoding (B); and (8) a method for screening an individual for a predisposition to a disorder in which DNA repair plays a role, comprising determining from a sample taken from the individual the presence or absence of a defect in **XRCC4** and/or **DNA ligase IV** activity.

USE - Compounds which modulate the interaction between **XRCC4**, **DNA ligase IV** and DPK can be used to modulate cellular DNA repair activity, e.g. in the treatment of proliferative disorders, cancers and tumours, disorders involving retroviruses such as AIDS, human adult T-cell leukaemia/lymphoma, Type I diabetes and multiple sclerosis, and also in radiotherapy and chemotherapy. They can also be used in the potentiation of gene targeting and gene therapy. They can also be used for the modulation of immune system function.

Dwg.0/6

FS CPI EPI
FA AB
MC CPI: B04-E02F; **B04-L08**; B11-C08; **B12-K04F**; B14-A02; B14-F09; B14-G02D; B14-H01; B14-S01; D05-H09; D05-H12A; D05-H17A2
EPI: **S03-E14H**; **S03-E14H5**

=>

=>

=> d his

(FILE 'HCAPLUS' ENTERED AT 12:17:46 ON 04 JAN 2001)
DEL HIS
E WO9830902/PN
L1 1 S E3
L2 2019 S DNA LIGASE
L3 53 S DNA LIGASE IV

```
     FILE 'REGISTRY' ENTERED AT 12:19:22 ON 04 JAN 2001
L4             1 S 9015-85-4
                 SEL CHEM

     FILE 'HCAPLUS' ENTERED AT 12:19:52 ON 04 JAN 2001
L5          1225 S L4
L6          3171 S E1-E24
L7            22 S POLYDEOXYRIBONUCLEOTIDE()(SYNTHETASE OR SYNTHASE)
L8             0 S POLYNUCLEOTIDE SYNTHASE
L9          3173 S L2,L3,L5-L8
                 E L1 AU
                 E JACKSON S/AU
L10           90 S E3,E19
L11          111 S E99,E109,E110
L12            1 S E123
                 E CRITCHLOW S/AU
L13            8 S E5,E9,E10
L14            6 S L9 AND L10-L13

     FILE 'REGISTRY' ENTERED AT 12:27:03 ON 04 JAN 2001
L15           85 S DNA LIGASE
L16           84 S L15 NOT L4

     FILE 'HCAPLUS' ENTERED AT 12:27:27 ON 04 JAN 2001
L17        10753 S L16
L18            2 S L17 AND L10-L13
L19            6 S L14,L18
L20           60 S XRCC4
L21            6 S L10-L13 AND L20
L22            5 S L19 AND L21
L23            2 S L19,L21 NOT L22
L24            7 S L22,L23
L25         3017 S DNA (L) LIGASE
L26          106 S DNA (L) LIGASE (L) IV
L27            1 S DNA (L) LIGASEIV
L28            6 S L10-L13 AND L25-L27
L29            7 S L24,L28
L30            9 S PKCS KU
L31            1 S L10-L13 AND L30
L32            7 S L29,L31
L33        14116 S L9,L17,L25-L27
L34            2 S L33 AND L30
L35           58 S L33 AND PK##
L36           28 S L33 AND KU
L37           36 S L30,L35-L36,L33 AND L20
L38            8 S L32,L34
L39           31 S L37 NOT L38
L40           39 S L38,L39
L41           39 S L40 AND DNA
L42            3 S L40 AND CDNA
L43            1 S L40 AND MRNA
L44            1 S L40 AND (DEOXYRIBONUCLE? OR RIBONUCLE?)
L45           39 S L40-L44
L46           23 S L20 NOT L45
L47           62 S L45,L46,L32,L38
L48           17 S L47 AND (PD<=19970113 OR PRD<=19970113 OR PRD.B<=19970113 OR
L49            4 S L29 NOT L48
L50           21 S L48,L49
L51           21 S L50 AND L9,L17,L20,L25-L27,L30
L52           11 S L50 AND (KU## OR PK##)
L53           21 S L51,L52
L54        14116 S L9,L17,L25-L27
L55        11791 S L54 AND (PD<=19970113 OR PRD<=19970113 OR PRD.B<=19970113 OR
L56           28 S L55 AND DRUG(S)SCREEN?
L57            4 S L56 AND L5
```

```
L58           3 S L56 AND L2
L59           1 S L56 AND L3
L60           4 S L56 AND L6
L61           0 S L56 AND L7
L62           7 S L56 AND L25-L27
L63           8 S L57-L62
L64           5 S L63 AND (ASSAYS OR KU(2W)REPAIR OR SCREENING)/TI
L65           3 S L64 NOT (RACEMASE OR AVIUM)/TI
L66          23 S L53,L65
L67          20 S L56 NOT L63,L66
L68          22 S L55 AND DRUG(S)DESIGN?
L69          46 S L68,L56
L70          38 S L69 NOT L63,L66
L71           2 S L70 AND LIGASE
L72          25 S L66,L71
                SEL RN L32

     FILE 'REGISTRY' ENTERED AT 12:58:09 ON 04 JAN 2001
L73           8 S E1-E8
L74           1 S 56-65-5
L75           6 S L73 NOT L74,L4
L76           3 S XRCC4
L77         125 S POLYDEOXYRIBONUCLEOTIDE (S) SYNTHETASE
L78           6 S L77 (S) IV
L79           9 S L76,L78
L80           2 S L75 NOT L79

     FILE 'HCAPLUS' ENTERED AT 13:01:51 ON 04 JAN 2001
L81           6 S L79
L82          28 S L72,L81
L83           3 S L82 NOT L72
L84          28 S L82,L83

     FILE 'HCAPLUS' ENTERED AT 13:03:20 ON 04 JAN 2001
                SEL HIT RN L84

     FILE 'REGISTRY' ENTERED AT 13:03:45 ON 04 JAN 2001
L85          11 S E9-E19

     FILE 'BIOSIS' ENTERED AT 13:04:29 ON 04 JAN 2001
L86        2981 S L9,L25-L27
L87        2096 S DNA(S)LIGASE?
L88        2981 S L86,L87
L89        2326 S L88 AND PY<=1997
                E JACKSON S/AU
L90         342 S E3,E24
L91          91 S E88,E94
                E CRITCHLOW S/AU
L92           9 S E3,E4,E6
L93           6 S L88 AND L90-L92
L94          54 S L20
L95           5 S L94 AND L93
L96           2 S L89 AND L93,L95
L97          34 S L88 AND L94
L98           2 S L97 AND L89
L99           3 S L96,L98
L100      69682 S L74
L101         78 S L100 AND L89
L102        196 S ATP AND L89
L103       5472 S ADENOSINE (1W) (TRIPHOSPHATE OR TRI PHOSPHATE)
L104          3 S L89 AND L103
L105        196 S L101,L102,L104
L106          9 S L105 AND IV
L107          8 S *108?/CC AND L106
L108          3 S L105 AND LIGASE IV
L109          6 S L99,L108
```

FILE 'BIOSIS' ENTERED AT 13:15:53 ON 04 JAN 2001

FILE 'EMBASE' ENTERED AT 13:16:06 ON 04 JAN 2001

L110	1019	S	L4
L111	1019	S	POLYDEOXYRIBONUCLEOTIDE SYNTHASE/CT
L112	845	S	L2,L3
L113	1767	S	L6
L114	1019	S	L7
L115	1303	S	L25-L27
L116	2148	S	L110-L115
L117	0	S	L79
L118	1585	S	L116 AND PY<=1997
L119	44	S	L20
L120	24	S	L116 AND L119
L121	1	S	L118 AND L120
L122	7	S	L120 AND 1998/PY
		E	DRUG/CT
L123	21	S	E148+NT/CT AND L118
L124	0	S	E176+NT/CT AND L118
L125	0	S	E200+NT/CT AND L118
L126	1	S	E273+NT/CT AND L118
L127	7	S	E298+NT/CT AND L118
L128	3	S	E364+NT/CT AND L118
L129	21	S	E369+NT/CT AND L118
L130	11	S	E408+NT/CT AND L118
L131	0	S	E482+NT/CT AND L118
L132	11	S	E645+NT/CT AND L118
L133	0	S	E693+NT/CT AND L118
L134	3	S	E842+NT/CT AND L118
L135	9	S	E902+NT/CT AND L118
L136	1	S	E924+NT/CT AND L118
L137	9	S	E923+NT/CT AND L118
L138	1	S	E937+NT/CT AND L118
		E	DRUG WASTE/CT
L139	55	S	L123-L138
L140	12	S	L139 NOT AB/FA
L141	43	S	L139 NOT L140
L142	22	S	L141 AND L110,L111
L143	47	S	L118 AND IV
L144	0	S	L143 AND L139
L145	2	S	L143 NOT AB/FA
L146	45	S	L143 NOT L145
L147	17	S	L111/MAJ AND L146
L148	11	S	L147 AND LIGASE/TI
L149	6	S	L147 NOT L148
L150	7	S	L143 AND LIGASE IV
L151	12	S	L148,L150

FILE 'EMBASE' ENTERED AT 13:37:08 ON 04 JAN 2001

FILE 'WPIDS' ENTERED AT 13:37:27 ON 04 JAN 2001

L152	193	S	L2
L153	2	S	L3
L154	24	S	L152 AND IV
L155	24	S	L153,L154
L156	1	S	XRCC4
L157	1	S	L152,L155 AND L156
L158	1206	S	C12N009-12/IC
L159	3	S	L152 AND L158
L160	0	S	L7
L161	224	S	L6
L162	224	S	L152-L155,L161
L163	13	S	G01N033/IC AND L162
L164	13	S	L157,L163
L165	528	S	(B04-B02C7 OR C04-B02C7 OR B04-L08 OR C04-L08)/MC

```
L166        732 S L162,L165
L167        111 S L166 AND G01N033/IC
L168         30 S L166 AND G01N033-50/IC
L169         18 S L166 AND G01N033-68/IC
L170         75 S L166 AND S03-E14H?/MC
L171        261 S L166 AND (B12-K04 OR B12-K04A? OR C12-K04 OR C12-K04A?)/MC
L172         94 S L166 AND (B12-K04F OR C12-K04F)/MC
L173        179 S L166 AND (B12-K04 OR B12-K04A OR C12-K04 OR C12-K04A)/MC
L174        326 S L167-L173
L175        215 SEA L174 AND N102/M0,M1,M2,M3,M4,M5,M6
L176        208 SEA L175 AND Q233/M0,M1,M2,M3,M4,M5,M6
L177         11 S L176 AND (ATP OR ADENOSINE (S) (TRIPHOSPHATE OR TRI PHOSPHATE
L178         11 S L176 AND PHOSPHORYL?
L179         52 S L176 AND BIND?
L180          1 S L176 AND KU##
L181          1 S L176 AND PKCS
L182          1 S L176 AND PK
L183          2 S L180-L182
L184          2 S L157,L183
L185          6 S L179 AND L177,L178
L186          1 S L184 AND L185

     FILE 'WPIDS' ENTERED AT 13:56:24 ON 04 JAN 2001
```